HHP/HPH COVID-19 Community Webinar Series

Monday, November 16, 2020

5:30pm – 6:30pm

Moderator – 11/16/20

Andy Lee, MD
Medical Director, *Hawai‘i Health Partners*
Chief of Staff, *Pali Momi Medical Center*
Hawai‘i Pacific Health

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- Specific areas may not pertain directly to your clinical practice area and/or may not be applicable to your practice based on your existing workflows, infrastructure, software (e.g. EHR), and communications processes.

Webinar Information

- You have been automatically muted.
  You cannot unmute yourself.
- You will be able to submit questions via the Q&A section.
  - Due to time constraints, any unanswered questions will be addressed this week and posted on the HHP website
- A recording of the meeting will be available tomorrow on the HHP website and intranet.

How to Claim CME Credit

1. Step 1: Confirm your attendance
   - You should have completed a brief questionnaire before joining today's live webinar.

2. Step 2: HPH CME team will email you instructions
   - Complete and submit evaluation survey that will be emailed to you within one week of the offering.
   - Your CE certificate will be immediately available to you upon completion of your evaluation.
   - Questions? Email hphcontinuingeduc@hawaiipacifichealth.org

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INTERPROFESSIONAL CONTINUING EDUCATION

Disclosures

- The planners and presenters of this activity report no relationships with companies whose products or services (may) pertain to the subject matter of this meeting

COVID-19 Updates

Melinda Ashton, MD
Executive Vice President
and Chief Quality Officer
Hawai'i Pacific Health

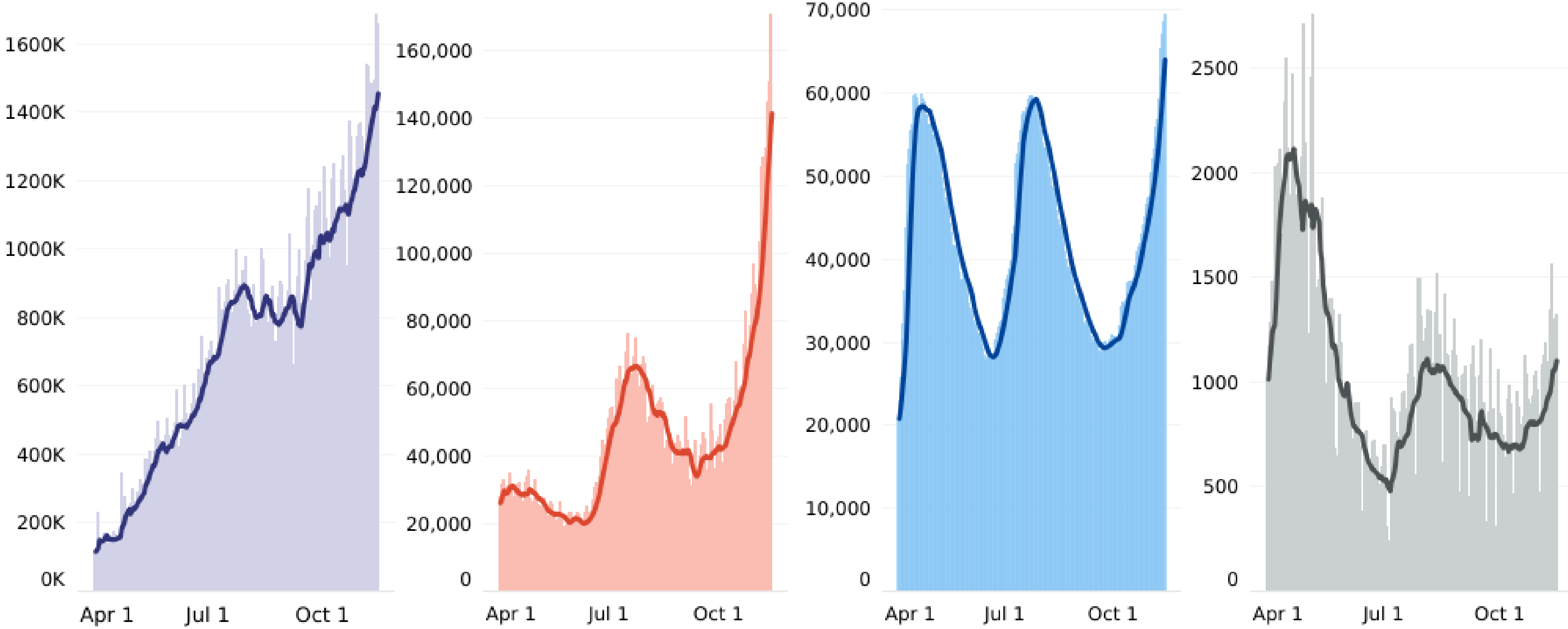
Douglas Kwock, MD
Vice President of
Medical Staff Affairs
Hawai'i Pacific Health

Gerard Livaudais, MD, MPH
Executive Vice President,
Population Health and
Provider Networks
Hawai'i Pacific Health

NATIONWIDE COVID-19 METRICS SINCE APRIL 1. 7-DAY AVERAGE LINES

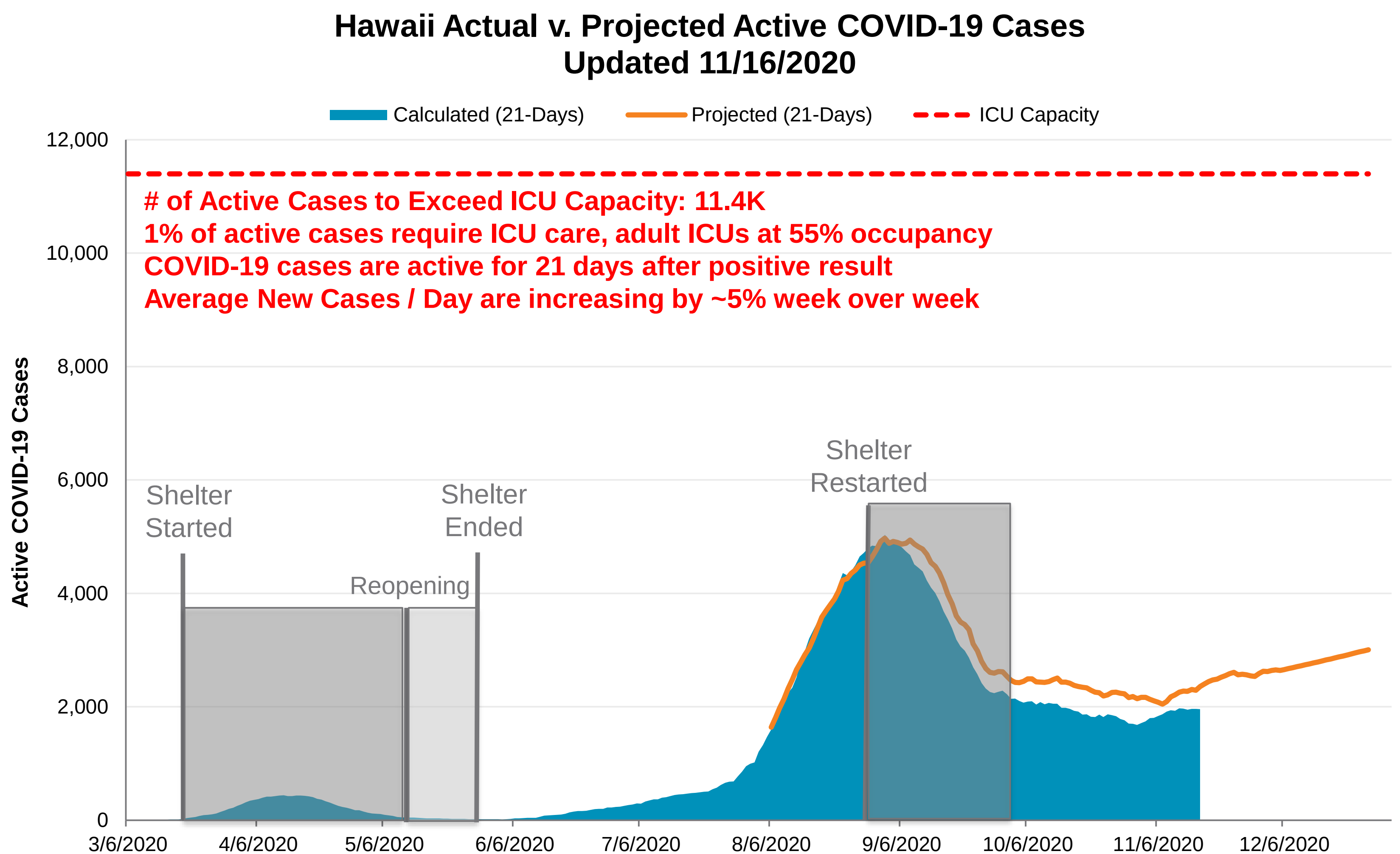
Choose Census Region
All

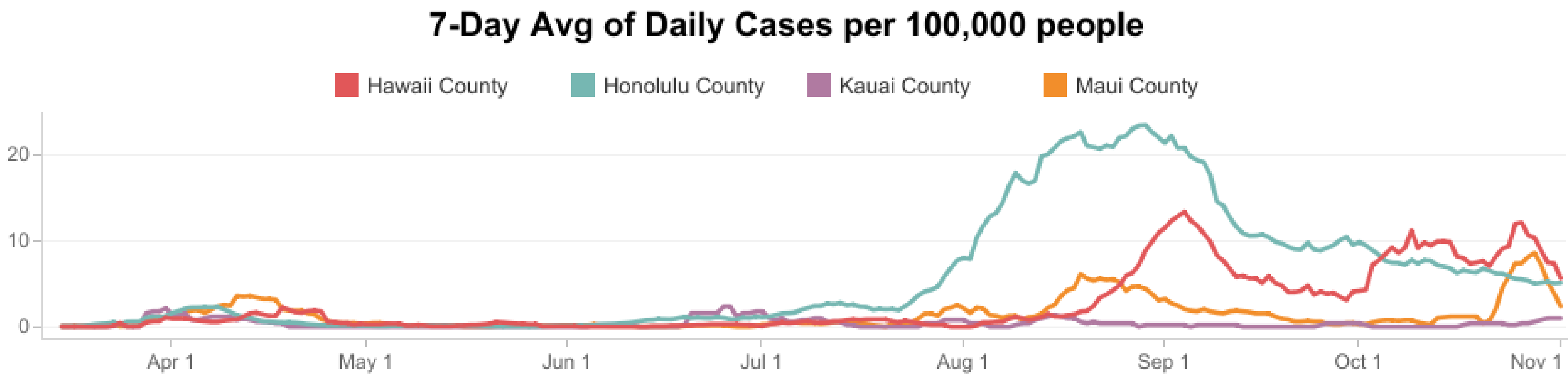
Daily Tests	Daily Cases	Currently Hospitalized	Daily Deaths
Nov 14: 1.66M	Nov 14: 163,473	Nov 14: 69,455	Nov 14: 1,321

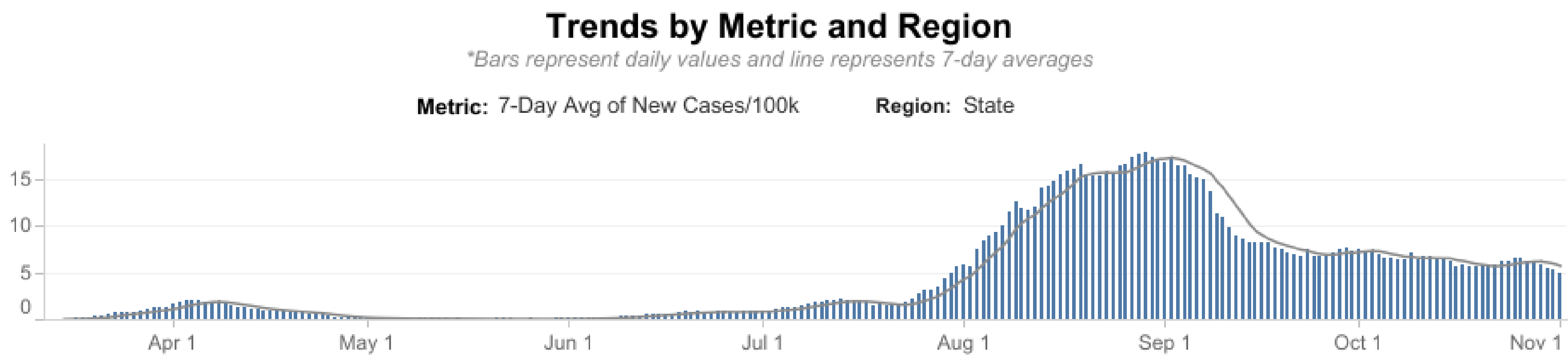


The COVID Tracking Project

Projected Active COVID-19 Cases







Last updated Nov 1

https://www.hawaiidata.org/covid19/#anchor1

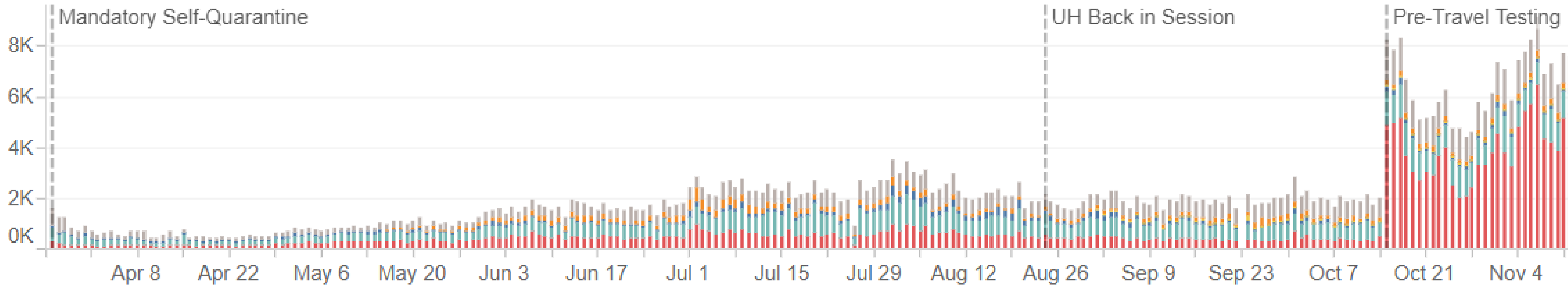
Region: State

Filter by Reason for Travel: (All)

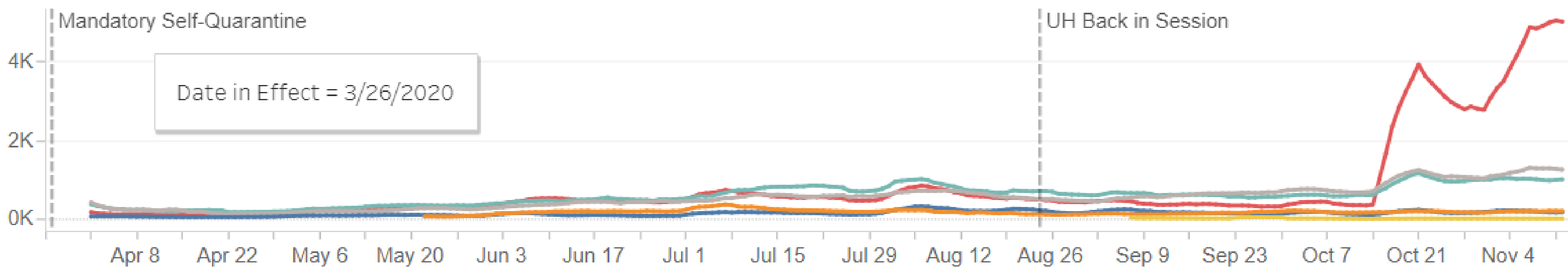
Reason for Travel: Visitor, Resident, New Resident, Attend School, Military, Other

Daily Arrivals – State

The average daily number of passangers arriving in Hawaii last year was roughly 30,000



7-day Averages – State



https://www.hawaiidata.org/covid19/#anchor1

COVID-19 Epi Curve*, Hawaii 2020

Updated November 16, 2020

Select County

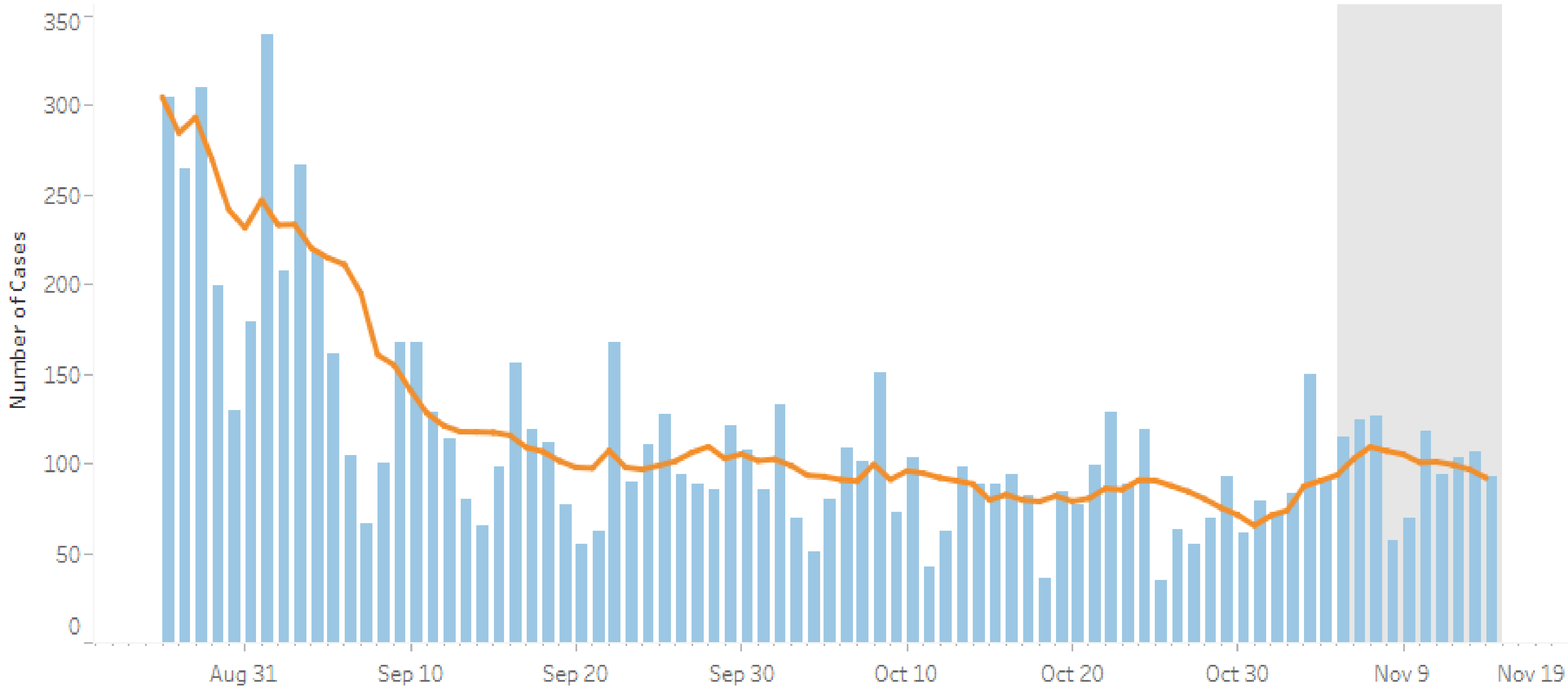
Statewide

92

Average cases/day (past 7 days)

16,468

Total Cases



*Illnesses that began in the past 10 days may not yet have been reported;
Includes all cases diagnosed in the state (non-residents and residents)

https://health.hawaii.gov/coronavirusdisease2019/what-you-should-know/current-situation-in-hawaii/

COVID-19 Testing*, Hawaii 2020

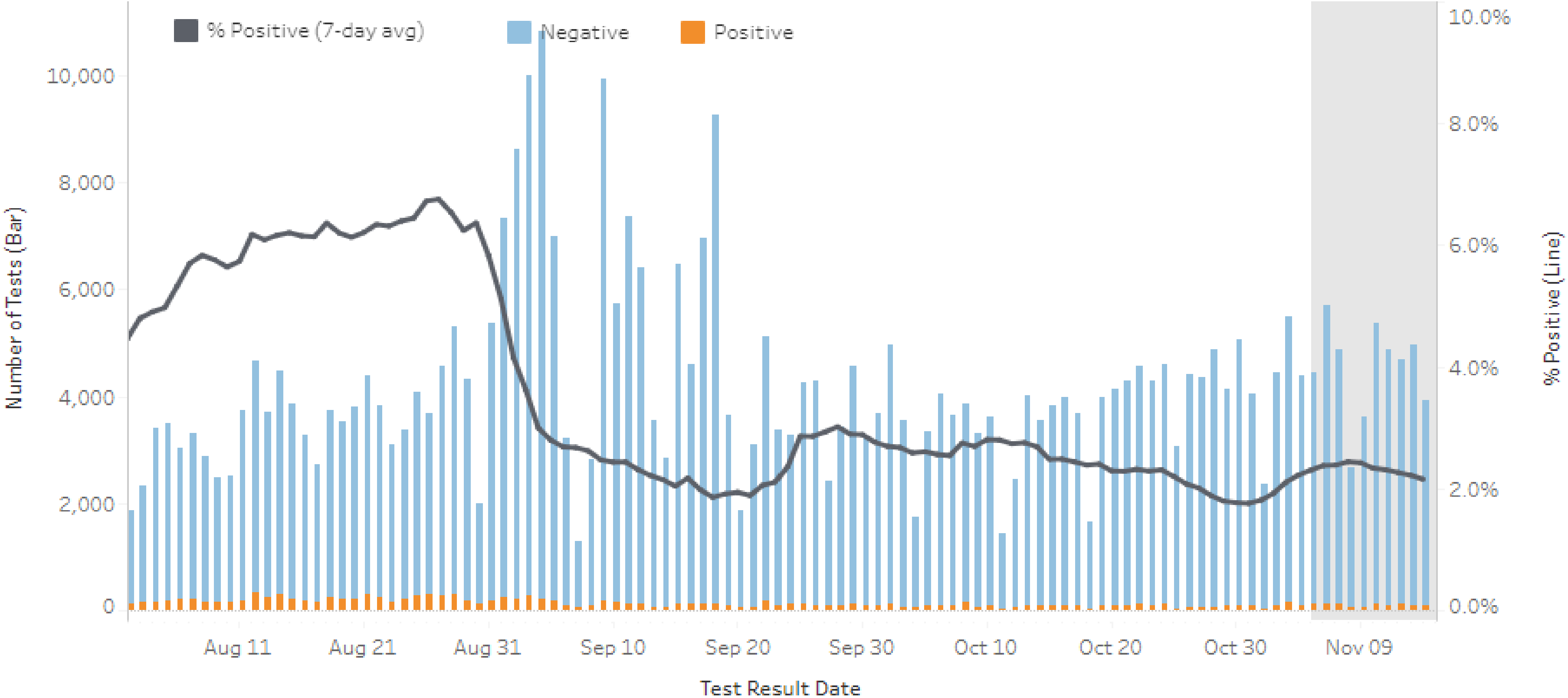
Updated November 16, 2020

Filter by County: (All)

Filter by Surge: (All)

4,304
Average Daily Tests Performed
(past 7 days)

2.2%
Percent Positive
(past 7 days)



* Illnesses that began in the past 10 days may not yet have been reported
Data as of 11:59pm November 14, 2020

Turnaround Time

https://health.hawaii.gov/coronavirusdisease2019/what-you-should-know/current-situation-in-hawaii/

As of 11/16/20	Total Census	ICU beds occupied	# Ventilators in use	# New Admissions w/ positive COVID-19	# Patients currently hospitalized w/ suspect or confirmed COVID-19	# Patients currently on a ventilator w/ confirmed COVID-19	# Patients currently in ICU w/ confirmed COVID-19
KMCWC	145	AICU: 0 NICU: 59 PICU: 4	AICU: 0 NICU: 16 PICU: 2	0	S: 1 C: 1	0	0
PMMC	95	15	8	0	S: 0 C: 8	1	1
SMC	121	13	7	0	S: 2 C: 2	0	0
WMC	50	3	1	0	S: 2 C: 2	0	0

S = Suspected; C= Confirmed

Focus Group Participants Needed for Phase 1a of COVID-19 Vaccination

- The Hawaiʻi Department of Health along with Olomana Loomis ISC will be conducting focus groups with health care professionals and first responders to understand their thoughts about a COVID-19 vaccine
  - November 16 – 21
  - Online via Zoom
  - Approximately 1 hour
  - Various time slots offered during the daytime and the evening

- If you are interested in signing up, please see the link below: https://forms.gle/dayRtRHagzF59rr79
  - *Please note: signing up does not mean participation is guaranteed*

MICHIGAN MEDICINE
UNIVERSITY OF MICHIGAN

OncCOVID Models

OncCOVID | OncCOVID(+) | Methods | Acknowledgements

- Patient Characteristics
- Cancer Characteristics
- Community COVID-19 Data

Treatment Information

- Immediate Treatment
- Delay

Adv

- Chan
- Chan

Dela

- Table
- Litera

☐ Check here if the patient lives in a different county (US only), state/province, or country from the treatment center.

Select Country

US

Select State/Province

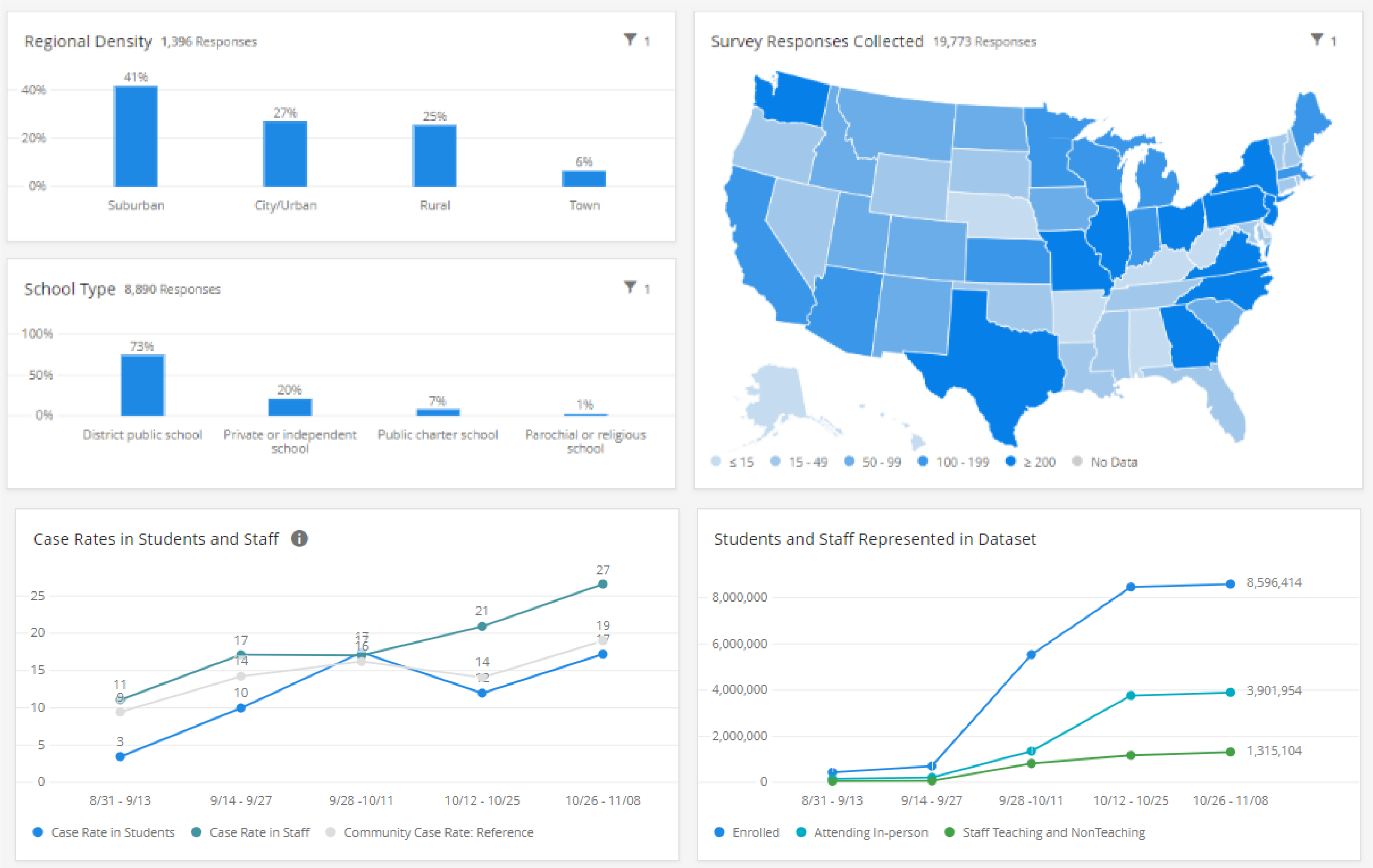
Hawaii

These results are for a 60 year old patient with stage II Colon cancer being treated and living in Honolulu, Hawaii, US.

Mortality Estimates | Survival Plots | Community Data

	Immediate Treatment	Delay Treatment
Risk of contracting COVID-19 in the next 6 month(s) (%)	18.27	14.43
COVID-19 mortality in the absence of cancer mortality in the next 6 month(s) (%)	0.67	0.53
Cancer mortality in the absence of COVID-19 in the next 5 year(s) (%)	13.77	13.77
Overall mortality in the absence of COVID-19 in the next 5 year(s) (%)	23.61	23.61
Overall mortality in the next 5 year(s) (%)	24.12	24.02

http://onccovid.med.umich.edu/



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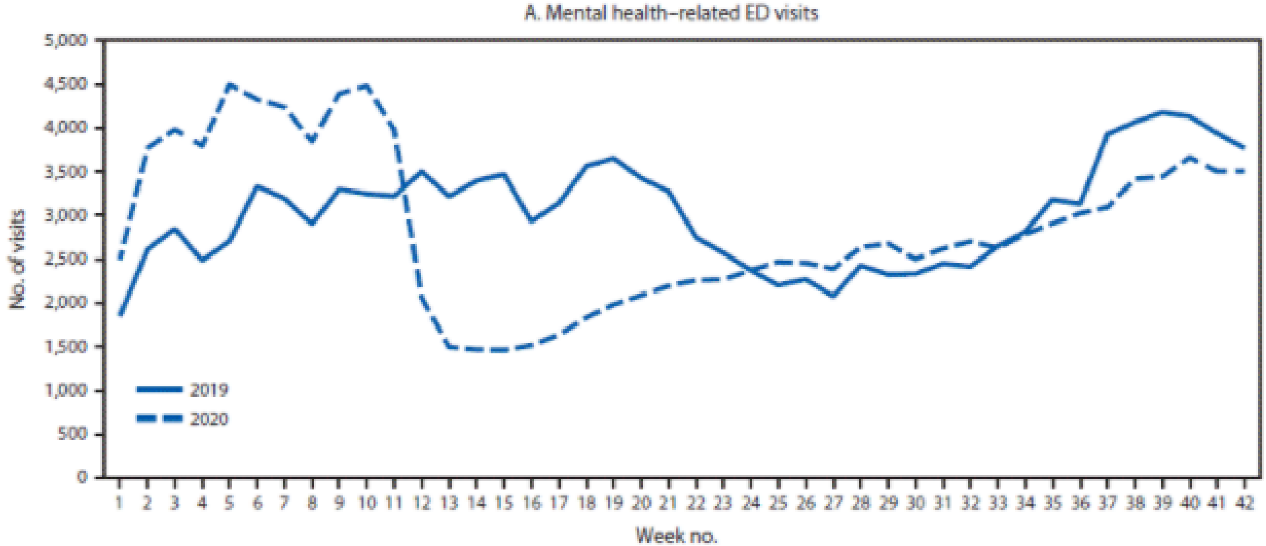
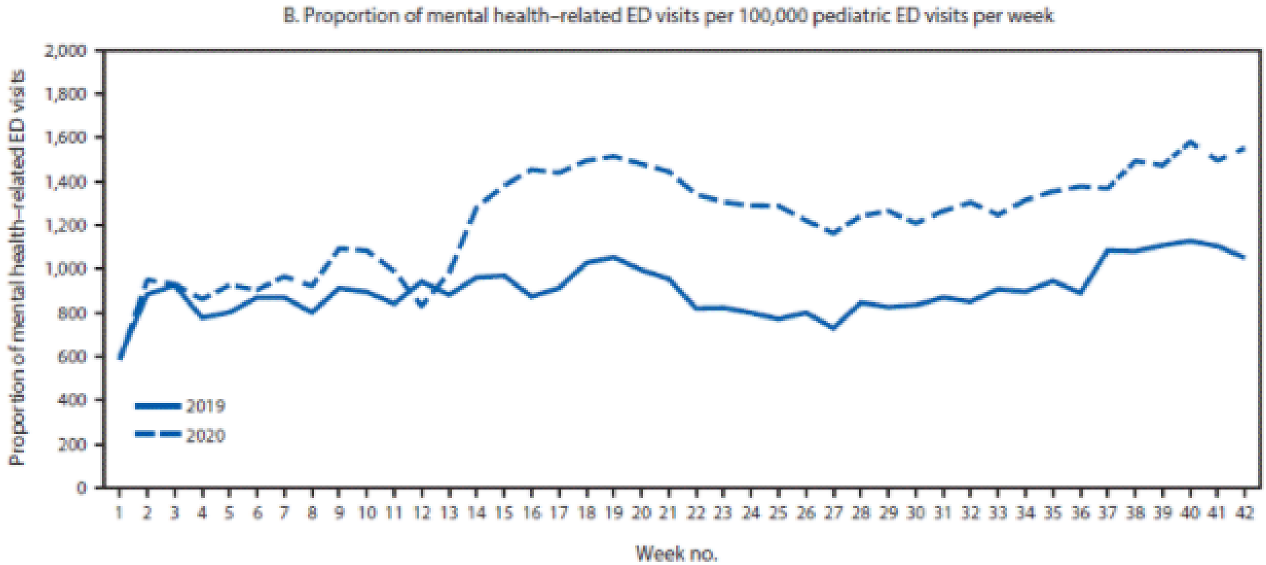
Weekly number of ED mental health–related visits (A) and proportion of (B) children's mental health–related ED visits per total ED visits among children aged <18 y/o





Mental Health–Related Emergency Department Visits Among Children Aged <18 Years During the COVID-19 Pandemic — United States, January 1–October 17, 2020. MMWR. https://www.cdc.gov/mmwr/volumes/69/wr/mm6945a3.htm?s_cid=mm6945a3_w#F1_down

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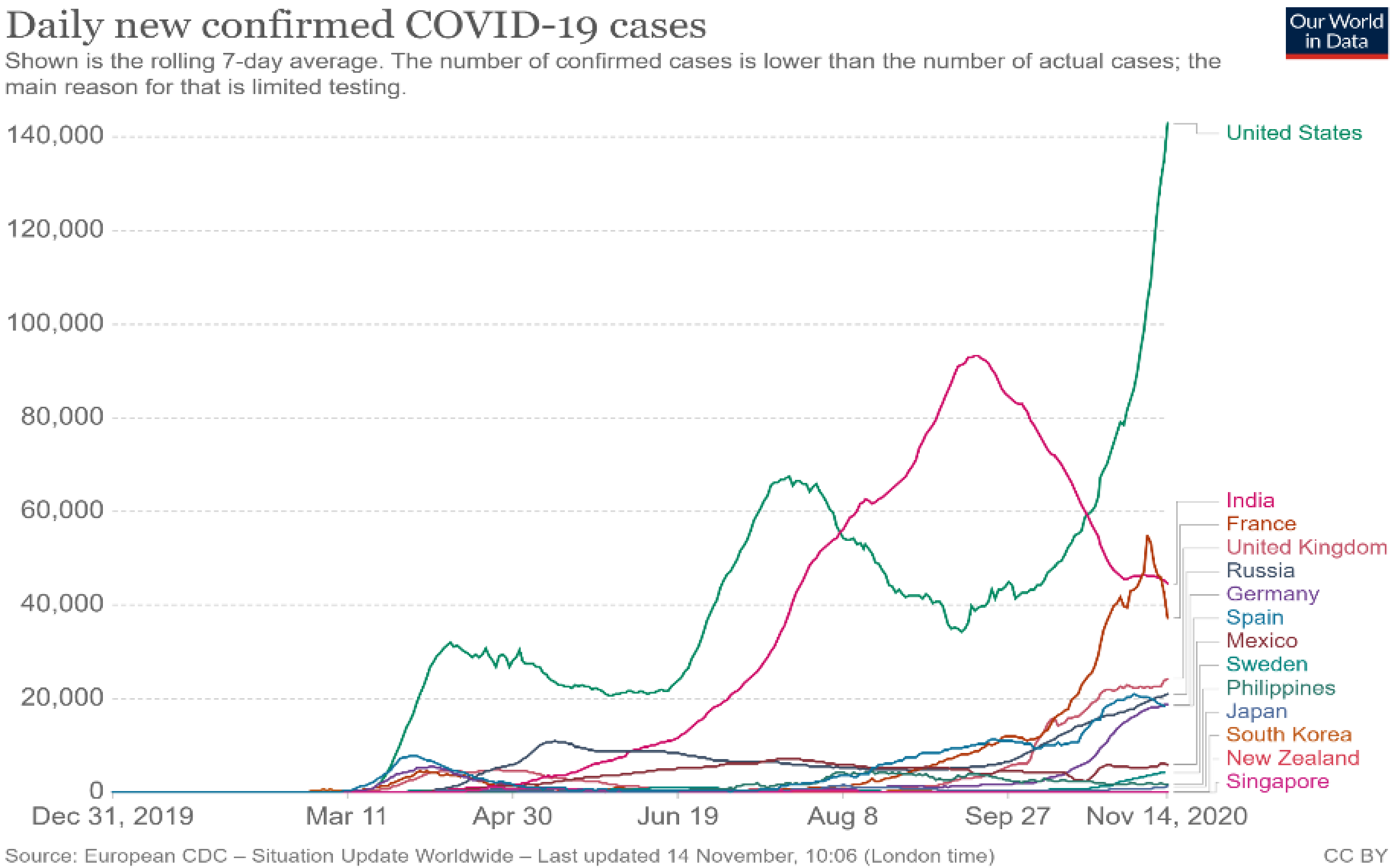
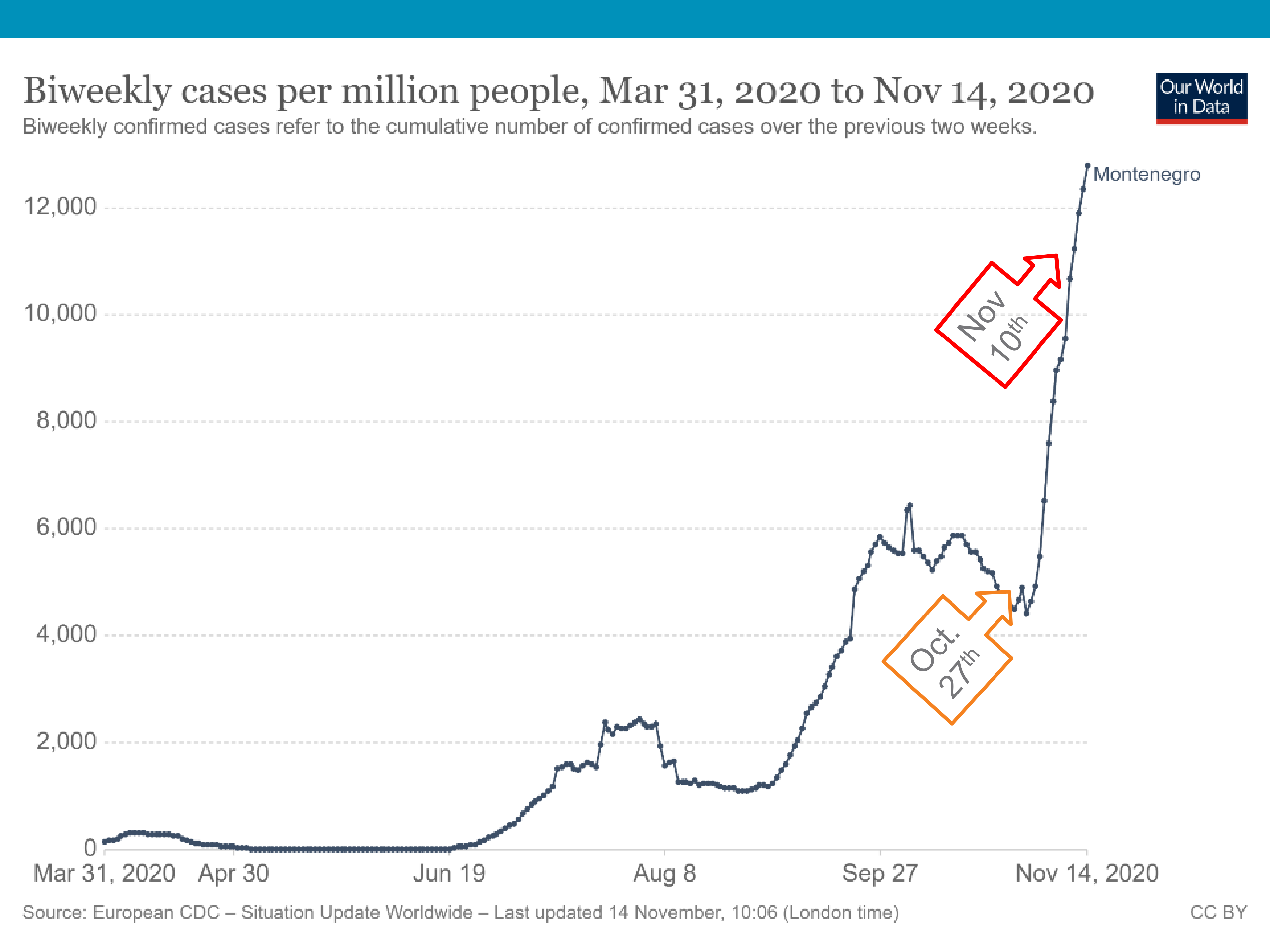
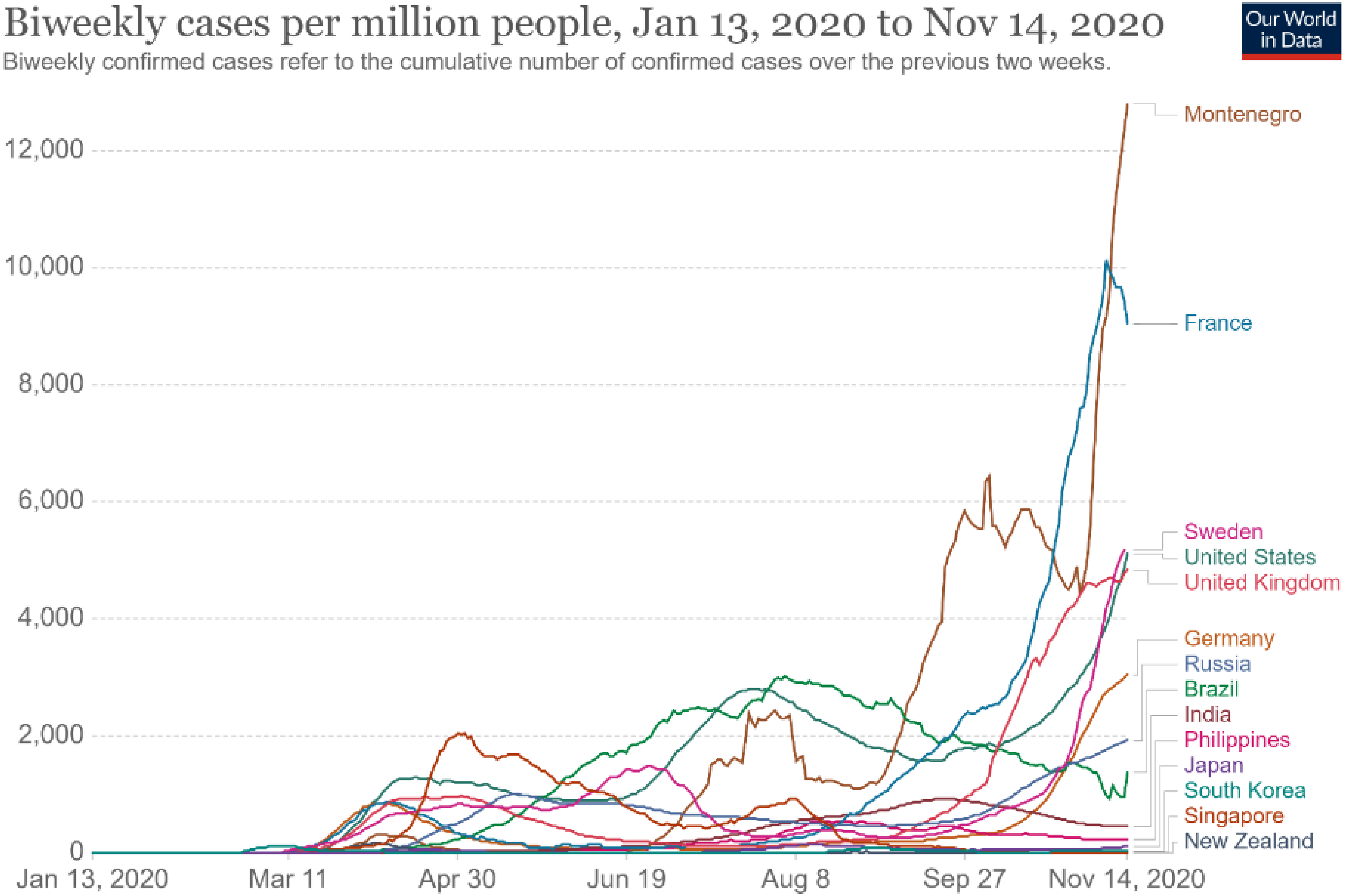

Daily new confirmed COVID-19 cases
Shown is the rolling 7-day average. The number of confirmed cases is lower than the number of actual cases; the main reason for that is limited testing.
Our World in Data
140,000
120,000
100,000
80,000
60,000
40,000
20,000
0
Dec 31, 2019
Mar 11
Apr 30
Jun 19
Aug 8
Sep 27
Nov 14, 2020
United States
India
France
United Kingdom
Russia
Germany
Spain
Mexico
Sweden
Philippines
Japan
South Korea
New Zealand
Singapore
Source: European CDC – Situation Update Worldwide – Last updated 14 November, 10:06 (London time)
CC BY



Biweekly cases per million people, Mar 31, 2020 to Nov 14, 2020
Biweekly confirmed cases refer to the cumulative number of confirmed cases over the previous two weeks.
Our World in Data
Montenegro
12,000
10,000
8,000
6,000
4,000
2,000
0
Mar 31, 2020
Apr 30
Jun 19
Aug 8
Sep 27
Nov 14, 2020
Nov 10th
Oct. 27th
Source: European CDC – Situation Update Worldwide – Last updated 14 November, 10:06 (London time)
CC BY

Biweekly cases per million people, Jan 13, 2020 to Nov 14, 2020

Biweekly confirmed cases refer to the cumulative number of confirmed cases over the previous two weeks.



Source: European CDC – Situation Update Worldwide – Last updated 14 November, 10:06 (London time)

Be Thankful and Thoughtful

Avoid the 3 Cs:

Closed spaces with poor ventilation

Crowds

Close contact with people outside your social bubble

Diabetes and COVID-19

Cindy Pau, MD

Internal Medicine/Endocrinology, Diabetes, & Metabolism, Diabetes & Hormone Center of the Pacific

Clinical Trials Investigator, East West Medical Research Institute

Assistant Clinic Professor of Medicine, John A. Burns School of Medicine, University of Hawaiʻi

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My Diabetic Patients with COVID-19

PATIENT A

- Age 64
- BMI 26
- A1c 7.2% (typically < 7%, increased in pandemic)
- Other comorbidities: Hypertension, Hyperlipidemia
- DM meds: Jardiance, Januvia, Glipizide ER, rosuvastatin, gemfibrozil,
- Overall fitness: Good fitness, highly mobile/active, goes surfing frequently, exercises regularly

PATIENT B

- Age 56
- BMI 45 (initial BMI 52)
- A1c 8.0% (typically 8-12%; less than 9% in past year)
- Other comorbidities: Mild Cardiomyopathy (EF 40%), Hypertension, Hyperlipidemia, NASH, OSA
- Notable meds: Jardiance, Tresiba, Ozempic, lisinopril, furosemide, metoprolol ER, rosuvastatin, omeprazole
- Overall fitness: Poor, sedentary lifestyle, zero exercise

ONLY ONE OF THEM SURVIVED…

It was Patient B…

What?

Why?

How?

No!!!

Objectives

- To understand that diabetes is a risk factor for increased COVID-19 morbidity and mortality

- To explore potential mechanisms mediating these risks

- To explore controversies regarding diabetes pharmacotherapy in patients with COVID-19

- Is there anything that patients and doctors can do to prevent poor outcomes in our diabetic patients in context of SARS-CoV-2 infection?

Prevalence of Diabetes in Acute Respiratory Syndrome Due to Coronaviruses is High

- Aggressive acute respiratory syndromes are produced by 3 coronaviruses
  - Severe Acute Respiratory Syndrome Coronavirus type 1 (SARS-CoV-1) [2002-2003; Guangdon, China]
  - Middle East Respiratory Syndrome Coronavirus (MERS-CoV) [2012; Saudi Arabia]
  - Severe Acute Respiratory Syndrome Coronavirus type 1 (SARS-CoV-2) [2019- ; Wuhan, China]

A systematic review & meta-analysis of the prevalence of diabetes mellitus and mortality due to Coronaviruses infection

	SAR-CoV-1	MERS-CoV	SARS-CoV-2
Diabetes prevalence in infected patients	9%	45%	10%
Mortality rate in infected patients with underlying diabetes	6%	36%	10%

*** Mortality in overall population is < 5% in most case series for SARS-CoV-2 infection*

Pinedo-Torres et al. Clin Med Ins: Endocrinology & Diabetes. 2020.

Diabetes Associated with Increased Morbidity and Mortality in Patients with COVID-19

A. Kumar et al. / Diabetes & Metabolic Syndrome: Clinical Research & Reviews 14 (2020) 535–545

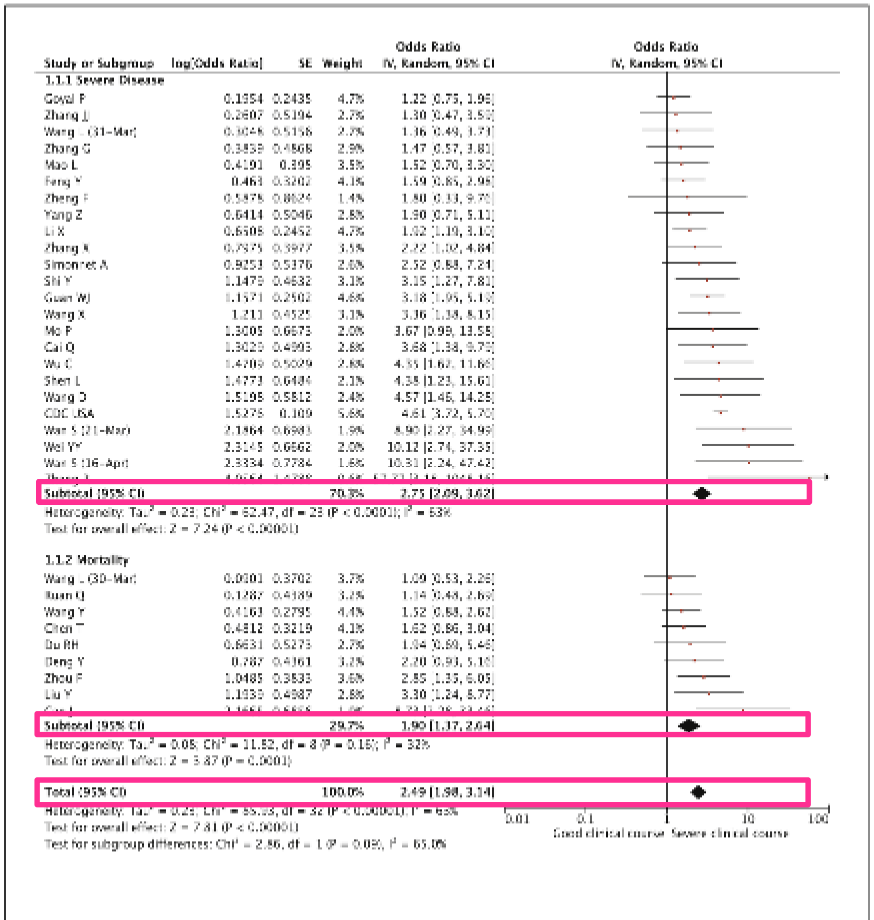


Fig. 3. Forest plot showing pooled odds ratio of diabetes mellitus associated with severe clinical course including mortality.

Meta-analysis

- 33 studies
- 16,003 patients
  - China: 8849 (55%) patients
  - USA: 7030 (44%) patients
  - France: 124 (1%) patients

- **Diabetes pooled prevalence: 1724 (11.2%)**
- Higher age = higher prevalence of diabetes

- Pooled OR for severe disease (ARDS, ICU, Mech Ven, ECMO): 2.75, p<0.01
- Pooled OR for mortality with DM: 1.90, p< 0.01
- Pooled OR for severe disease or mortality: 2.49, p<0.01

Demographic and Clinical Characteristics of Patients in the First 24 Hours of ICU Admission for COVID-19 in Lombardy, Italy

	Patients by age, y, No. (%)								
	All	0-20	21-40	41-50	51-60	61-70	71-80	81-90	91-100
No. (%)	1591 (100)	4 (<1)	56 (4)	143 (9)	427 (27)	598 (38)	341 (21)	21 (1)	1 (<1)
Age, median (IQR), y	63 (56-70)	16 (14-19)	34 (31-38)	47 (44-49)	56 (54-59)	65 (63-68)	74 (72-76)	83 (81-84)	91
Males	1304 (82)	3 (75)	44 (79)	119 (83)	355 (83)	484 (81)	279 (82)	19 (90)	1 (100)
Females	287 (18)	1 (25)	12 (21)	24 (17)	72 (17)	114 (19)	62 (18)	2 (10)	0
Comorbidities, No. with data	1043	2	35	82	273	380	253	1	1
None	334 (32)	0	23 (66)	50 (61)	107 (39)	107 (28)	47 (19)	0	0
Hypertension	509 (49)	0	4 (11)	21 (26)	121 (44)	195 (51)	156 (62)	12 (75)	0
Cardiovascular disease[a]	223 (21)	0	1 (3)	4 (5)	43 (16)	87 (23)	81 (32)	6 (38)	1 (100)
Hypercholesterolemia	188 (18)	0	1 (3)	1 (1)	30 (11)	92 (24)	59 (23)	5 (31)	0
Diabetes, type 2	180 (17)	0	1 (3)	4 (5)	40 (15)	86 (23)	46 (18)	3 (19)	0
Malignancy[b]	81 (8)	0	0	2 (2)	10 (4)	33 (9)	33 (13)	3 (19)	0
COPD	42 (4)	0	1 (3)	0	8 (3)	12 (3)	20 (8)	1 (6)	0
Chronic kidney disease	36 (3)	0	0	2 (2)	10 (4)	17 (4)	7 (3)	0	0
Chronic liver disease	28 (3)	0	0	2 (2)	8 (3)	13 (3)	5 (2)	0	0
Other[c]	205 (20)	3 (100)	6 (17)	10 (12)	49 (18)	77 (20)	55 (22)	5 (31)	0
Respiratory support, No.	1300	2	46	108	351	487	287	18	1
Invasive mechanical ventilation	1150 (88)	2 (100)	37 (80)	87 (81)	315 (90)	449 (92)	246 (86)	14 (78)	0
Noninvasive ventilation	137 (11)	0	8 (17)	16 (15)	33 (9)	36 (7)	39 (14)	4 (22)	1 (100)
Oxygen mask	13 (1)	0	1 (2)	5 (5)	3 (1)	2 (<1)	2 (1)	0	0
PEEP, cm H_2O									
No.	1017	2	33	81	278	377	234	11	1
Median (IQR)	14 (12-16)	9.5 (5-14)	14 (10-15)	14 (12-15)	14 (12-15)	14 (12-16)	14 (12-15)	12 (8-15)	10
FiO_2, %									
No.	999	2	31	81	270	375	228	11	1
Median (IQR)	70 (50-80)	40 (30-50)	60 (50-70)	60 (50-80)	65 (50-80)	70 (55-80)	70 (50-80)	60 (50-90)	60
PaO_2/FiO_2 ratio									
No.	781	2	26	58	213	306	169	7	0
Median (IQR)	160 (114-220)	259 (195-323)	201.5 (123-248)	168.5 (112-260)	163 (120-230)	152.5 (110-213)	163 (120-205)	150 (86-250)	NA
Prone position, No./total (%)	240/875 (27)	0/2	3/25 (12)	24/71 (34)	70/247 (28)	90/337 (27)	51/187 (27)	2/6 (33)	NA
ECMO, No./total (%)	5/498 (1)	NA	0/15	0/42	2/149 (1)	3/193 (2)	0/95	0/4	NA

DM Prevalence Higher in Critically Ill Patients with COVID-19

- Retrospective case series of 1591 consecutive patients with laboratory-confirmed COVID-19 referred for **ICU admission in Italy**
  - **DM prevalence: 17%**
- Overall in the literature: prevalence of DM in patients with COVID-19: **5-20%**

DM Prevalence Higher in Critically Ill Patients with COVID-19

- Clinical features in critically ill patients infected with SARS-CoV-2 in China outside of Wuhan:
  - Overall mortality: 33%
  - **Diabetes Prevalence: 22%**
  - Mortality rates in patients with underlying diabetes: 45.5%

Int J Diabetes Dev Ctries

Table 1 Demographics and baseline characteristics of critically ill patients with COVID-19

Items	All patients (n = 49)	Survivors (n = 33)	Deceased (n = 16)	p value
Age, years	63 (53–73)	58 (50–74)	67 (60–72)	0.267
Sex, n (%)				
Female	17 (35)	12 (36)	5 (31)	0.724
Male	32 (65)	21 (64)	11 (69)	
Exposure history, n (%)				
Familiar/cluster infections	26 (53)	16 (48)	10 (63)	0.357
Community infections	23 (47)	17 (52)	6 (37)	0.357
Occupation, n (%)				
Agricultural worker	13 (27)	9 (27)	4 (25)	0.867
Employee	11 (22)	8 (24)	3 (19)	0.669
Retiral	25 (51)	16 (49)	9 (56)	0.610
Smokers, n (%)	18 (37)	11 (33)	7 (44)	0.478
Chronic systemic diseases, n (%)	36 (73)	22 (67)	14 (88)	0.174
Hypertension	22 (45)	13 (39)	9 (56)	0.266
Chronic heart disease	16 (33)	10 (30)	6 (38)	0.614
T2DM	11 (22)	6 (18)	5 (31)	0.456
Chronic obstructive pulmonary disease	11 (22)	8 (24)	3 (19)	1.000
Cerebrovascular disease	9 (18)	4 (12)	5 (21)	0.130
Chronic liver disease	5 (10)	4 (12)	1 (6)	1.000
Chronic renal disease	2 (4)	1 (3)	1 (6)	1.000
Malignancy	2 (4)	1 (3)	1 (6)	1.000
Two or more of the above diseases	28 (57)	15 (45)	13 (81)	0.018
Days from disease onset to admission, days	7.0 (4.5–10.0)	6.0 (4.0–10.0)	8.0 (6.3–10.8)	0.534
Days from admission to critical condition, days	4.0 (2.5–8.0)	6.0 (3.5–8.5)	2.5 (1.0–4.0)	0.001

Data are shown as median (IQR) or n (%). p values comparing survivors and deceased are from χ^2 test, Fisher's exact test, or Mann-Whitney U test. *COVID-19*, coronavirus disease 2019; *IQR*, interquartile range

Int J Diabetes Dev Ctries

Table 5 Comparison of outcomes between 11 diabetic and 38 nondiabetic critically ill COVID patients

Items	Diabetic (n = 11)	Nondiabetic (n = 38)	p value
Age, years	58 (51–62)	68 (53–75)	0.116
Sex, n (%)			
Female	4 (36)	13 (34)	1.000
Male	7 (64)	25 (66)	1.000
Blood routine			
Neutrophil percentage, (%) (normal range 40–75)	85.8 (71.5–91.5)	73.8(64.2–85.6)	0.045
Lymphocytes ($\times 10^9$/L; normal range 1.1–3.2)	0.7 (0.5–0.9)	0.9 (0.7–1.4)	0.168
Lymphocyte percentage, (%) (normal range 20–50)	8.5 (3.7–19.7)	16.9 (9.6–26.1)	0.042
Infection biomarkers			
C-reactive protein (mg/L; normal range 0.0–8.0)	27.8 (12.9–40.8)	40.7 (16.6–65.4)	0.297
Procalcitonin (ng/mL; normal range 0.0–0.5)	4.1 (0.2–7.9)	0.5 (0.1–1.6)	0.106
Blood biochemistry			
Fasting blood glucose (mmol/L; normal range 3.9–6.1)	10.7 (7.4–14.5)	6.1 (5.5–8.1)	0.001
Lactate dehydrogenase (U/L; normal range 109–245)	419.0 (326.0–523.8)	268.3 (203.3–431.2)	0.042
Prognosis			
Discharge, n (%)	6 (55)	27(71)	0.466
Death, n (%)	5 (45)	11 (29)	0.466

Data are shown as median (IQR) or n (%). p values comparing diabetic and nondiabetic COVID patients are from χ^2 test, Fisher's exact test, or Mann-Whitney U test. *COVID-19*, coronavirus disease 2019; *IQR*, interquartile range

CORONADO Study: Phenotypic Characteristics and Prognosis of COVID-19 Inpatients with Diabetes

Diabetologia (2020) 63:1500–1515 1503

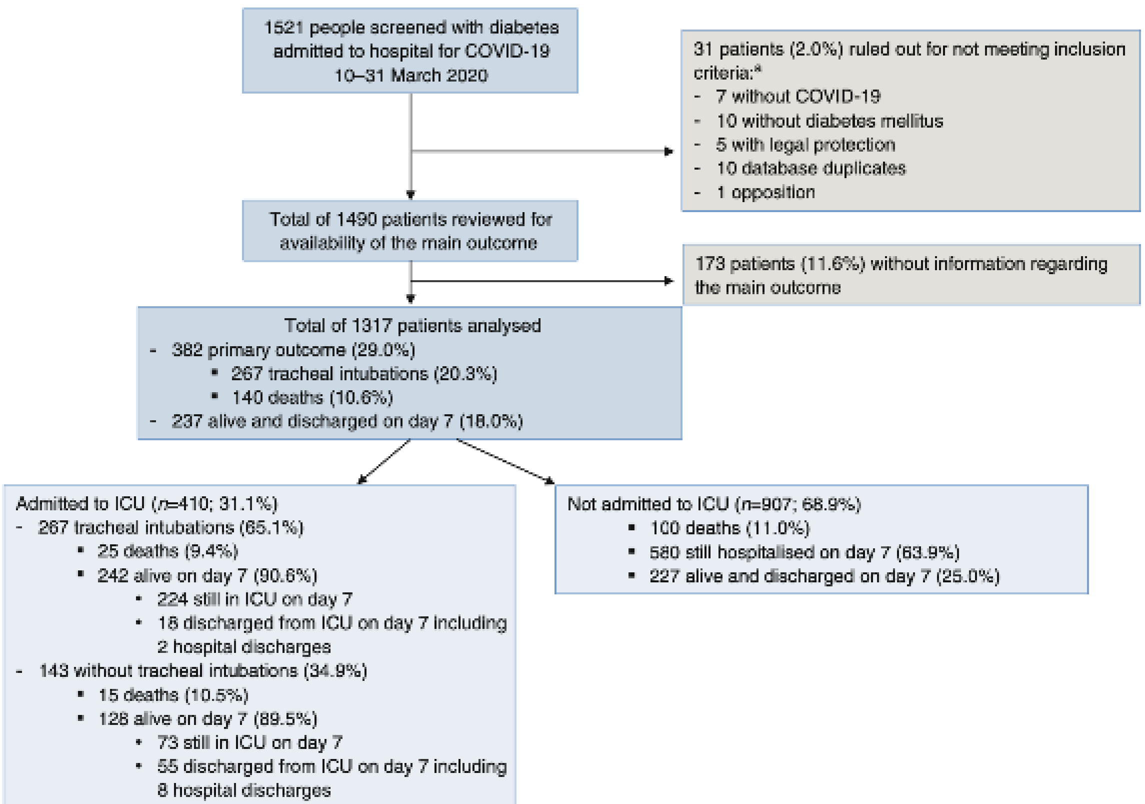


Fig. 1 Study flowchart. [a]Two patients ruled out for not meeting inclusion criteria were in two categories

Nationwide multi-center observational study in France

Primary outcome = death or intubation

Secondary outcome = death by day 7

CORONADO Study Findings:

Table 1 Clinical characteristics prior to admission of CORONADO participants, according to primary outcome (tracheal intubation and/or death within 7 days of admission), and death on day 7

Clinical features	Number of people with available data	All	Primary outcome ($n = 382$) OR (95% CI)	Death ($n = 140$) OR (95% CI)
Sex (female/male)	1317	462/1317 (35.1)	0.77 (0.60, 0.99)	0.80 (0.55, 1.17)
Age (years)[a]	1317	69.8 ± 13.0	1.00 (0.99, 1.01)	1.09 (1.07, 1.11)
Age class (years)	1317			
<55		159/1317 (12.1)	1	1
55–64		266/1317 (20.2)	0.58 (0.38, 0.90)	1.00 (0.23, 4.23)
65–74		394/1317 (29.9)	0.89 (0.60, 1.31)	3.22 (0.95, 10.1)
≥75		498/1317 (37.8)	0.85 (0.58, 1.24)	14.6 (4.56, 46.6)
Type of diabetes	1317			
Type 2		1166/1317 (88.5)	1	1
Type 1		39/1317 (3.0)	0.72 (0.35, 1.56)	0.44 (0.11, 1.86)
Other		71/1317 (5.4)	1.33 (0.80, 2.20)	1.50 (0.77, 2.93)
Diagnosed on admission		41/1317 (3.1)	0.79 (0.38, 1.63)	–
Ethnicity	1035			
EU		641/1035 (61.9)	1	1
MENA		196/1035 (18.9)	0.98 (0.69, 1.40)	0.87 (0.52, 1.47)
AC		174/1035 (16.8)	0.96 (0.66, 1.40)	0.78 (0.44, 1.37)
AS		24/1035 (2.3)	1.51 (0.65, 3.52)	–
BMI (kg/m^2)[a]	1117	28.4 [25.0–32.7]	1.25 (1.09, 1.42)	0.95 (0.78, 1.16)
BMI class	1117			
<25 kg/m^2		279/1117 (25)	1	1
25–29.9 kg/m^2		410/1117 (36.7)	1.32 (0.93, 1.89)	0.70 (0.42, 1.16)
30–39.9 kg/m^2		359/1117 (32.1)	1.71 (1.20, 2.43)	0.76 (0.45, 1.27)
≥40 kg/m^2		69/1117 (6.2)	1.28 (0.70, 2.32)	0.74 (0.29, 1.84)
Diabetes duration (years)	772	13.6 ± 10.9	1.00 (0.98, 1.01)	1.01 (0.99, 1.04)
HbA_{1c} (mmol/mol)[a]	846	65.4 ± 21.2	0.99 (0.99, 1.00)	1.00 (0.99, 1.02)
HbA_{1c} (%)[a]	846	8.1 ± 1.9	0.94 (0.86, 1.03)	1.02 (0.87, 1.19)
HbA_{1c} (categories)	846			
<53 mmol/mol (7%)		245/846 (29.0)	1	1
53–63 mmol/mol (7–7.9%)		228/846 (27.0)	0.84 (0.55, 1.27)	1.55 (0.82, 2.93)
64–74 mmol/mol (8–8.9%)		164/846 (19.4)	0.92 (0.59, 1.45)	1.09 (0.52, 2.28)
≥75 mmol/mol (9%)		209/846 (24.7)	0.78 (0.51, 1.21)	0.84 (0.40, 1.75)
Hypertension	1299	1003/1299 (77.2)	1.23 (0.92, 1.65)	1.82 (1.11, 2.98)
Dyslipidaemia	1255	640/1255 (51.0)	1.07 (0.84, 1.37)	1.21 (0.84, 1.74)
Tobacco use	1029			
Never		582/1029 (56.6)	1	1
Former		390/1029 (37.9)	1.21 (0.91, 1.61)	1.00 (0.64, 1.57)
Current		57/1029 (5.5)	1.54 (0.87, 2.74)	1.20 (0.49, 2.93)
Long-term diabetes complications				
Microvascular complications	883	413/883 (46.8)	1.28 (0.94, 1.73)	5.25 (3.03, 9.10)
Severe diabetic retinopathy	954	66/954 (6.9)	1.22 (0.71, 2.11)	2.05 (1.03, 4.07)
Diabetic kidney disease	1066	355/1066 (33.3)	1.03 (0.78, 1.37)	3.19 (2.09, 4.87)
History of diabetic foot ulcer	1232	76/1232 (6.2)	0.67 (0.38, 1.18)	1.53 (0.79, 2.99)
Macrovascular complications	1189	485/1189 (40.8)	1.18 (0.91, 1.52)	3.58 (2.41, 5.31)
Ischaemic heart disease (ACS/CAR)	1251	336/1251 (26.9)	1.04 (0.79, 1.37)	2.65 (1.84, 3.82)
Cerebrovascular disease (stroke or TIA)	1267	163/1267 (12.9)	1.02 (0.71, 1.47)	2.19 (1.4, 3.42)
Peripheral artery disease (major amputation/LLAR)	1285	145/1285 (11.3)	0.91 (0.61, 1.34)	1.97 (1.23, 3.17)

- A1c did not correlate with COVID-severity
- ↑Age, microvascular and macrovascular DM complications were associated with risk of early death in patients with diabetes hospitalized for COVID-19

Association ≠ Causation
Postulated Mechanisms?

Diabetic patients may have increased morbidity and mortality with COVID-19 because:

- Increased cell affinity and efficient virus entrance by overexpression of ACE2 receptors +/- DPP4
- Decreased viral clearance
- Immune suppressed: ↓ quantity and function of T-cells, ↓phagocytic activity
- Susceptibility to hyperinflammation by an increase of pro-inflammatory cytokines

Lukassen et al. EMBO J. 2020.
Kulcsar et al. JCI Insight. 2019.
Fang et al. Lancet Respir Med. 2020.

SARS-CoV-2 and ACE2

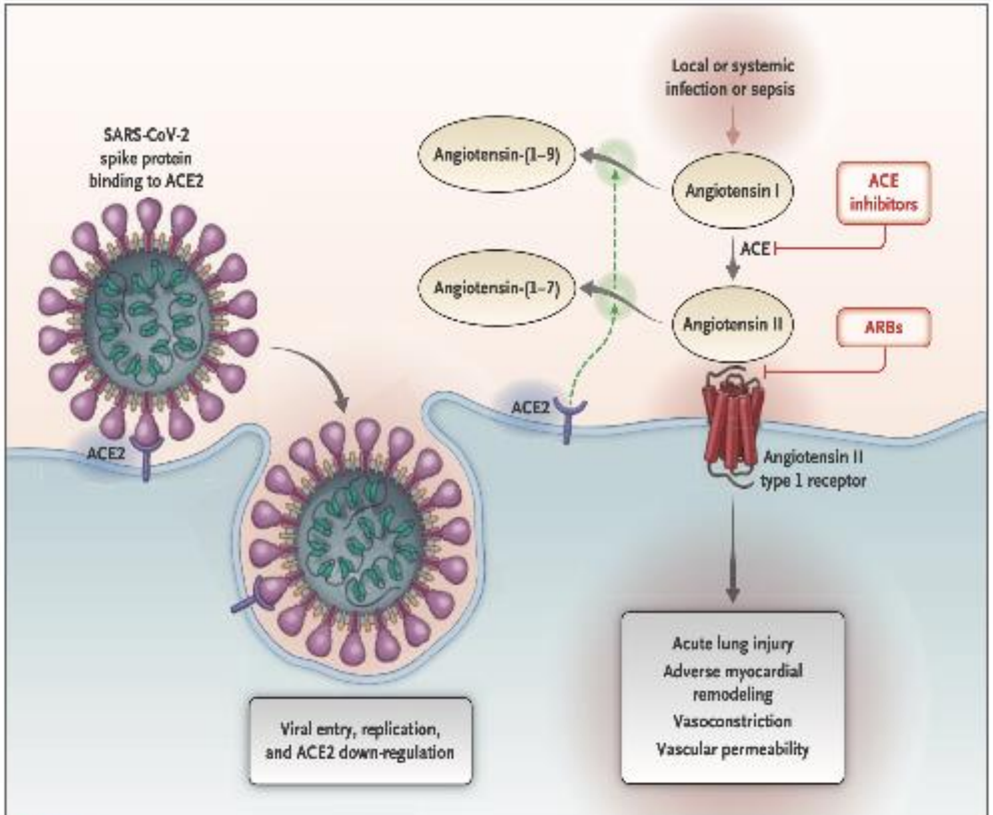


Figure 1. Interaction between SARS-CoV-2 and the Renin–Angiotensin–Aldosterone System.

Shown is the initial entry of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) into cells, primarily type II pneumocytes, after binding to its functional receptor, angiotensin-converting enzyme 2 (ACE2). After endocytosis of the viral complex, surface ACE2 is further down-regulated, resulting in unopposed angiotensin II accumulation. Local activation of the renin–angiotensin–aldosterone system may mediate lung injury responses to viral insults. ACE denotes angiotensin-converting enzyme, and ARB angiotensin-receptor blocker.

Context:

- Interaction between SARS viruses and ACE2 has been proposed as a potential factor for their infectivity.
- **Double trouble**: SARS-Cov-2 Down-regulates ACE2 expression -> ↑AngII
- Concerns about using RAAS inhibitors may alter ACE2
- Data is conflicting regarding whether ACEi increases ACE2 levels in animal models and human studies (*are plasma ACE2 levels, Ang-(1-7), urinary ACE2 levels good surrogates of membrane-bound ACE2 levels?)*
  - *Earlier studies: potentially harmful*
  - *Recent studies: probably beneficial*
- Data is lacking about effect of ACEi on lung-specific expression of ACE2

RAAS Inhibitors Associated with Lower Risk of Mortality in Hypertensive COVID-19 Patients: Systematic Review & Meta-Analysis

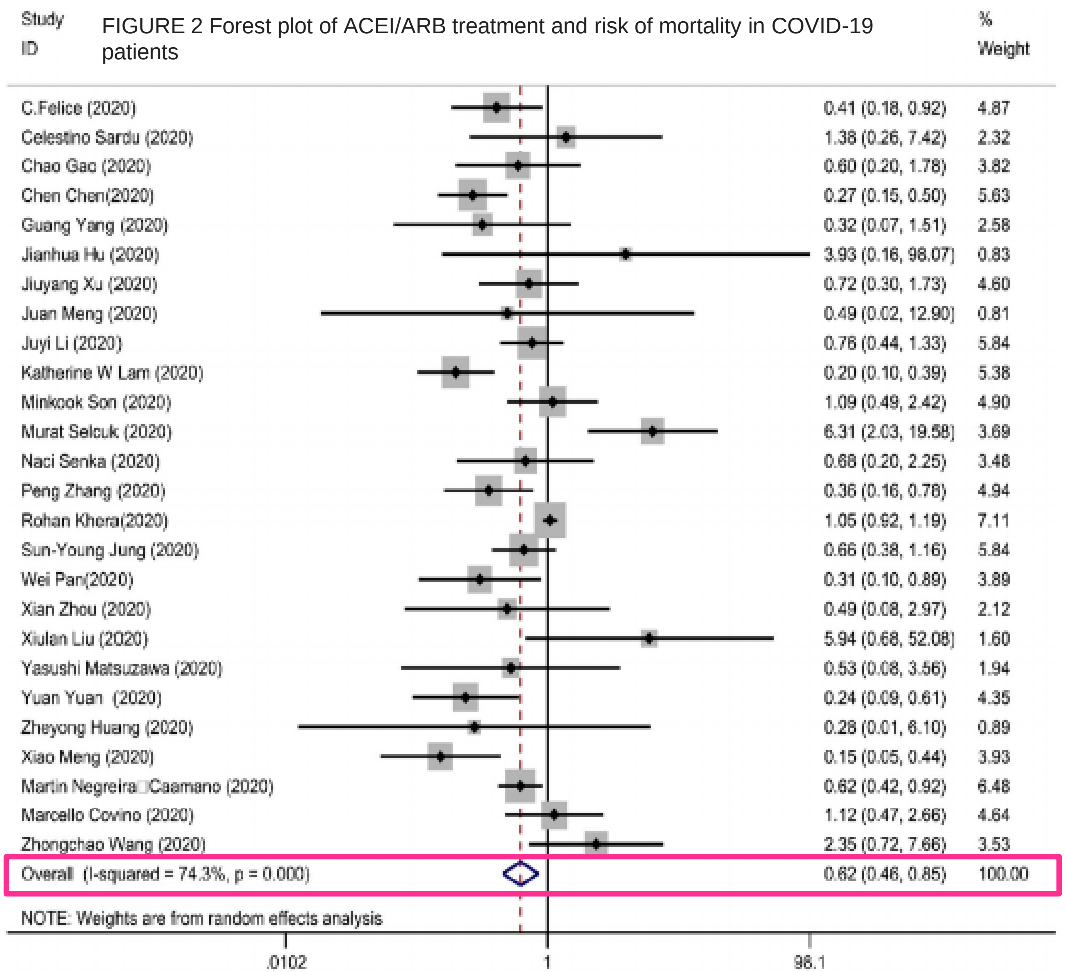


FIGURE 2 Forest plot of ACEI/ARB treatment and risk of mortality in COVID-19 patients

- 26 studies
- 8104 Hypertensive patients treated on ACEi/ARB
- 8203 hypertensive patients NOT on ACEi/ARB
- ACEi/ARB treatment associated with significantly lower risk of mortality
- *Suggests that ACEi/ARB medications should not be discontinued for hypertensive patients in context of COVID-19 pandemic*

Effects of ACEi/ARB treatment

Outcomes	*N* of studies	*N* of subjects	OR	95% CI	*p*	I^2
Ventilatory support	7	1734	0.682	0.475–1.978	.037	0.0%
Severity of COVID-19	10	2309	0.699	0.444–1.098	.120	80.0%
Admission to ICU	11	1912	0.704	0.460–1.078	.106	51.5%

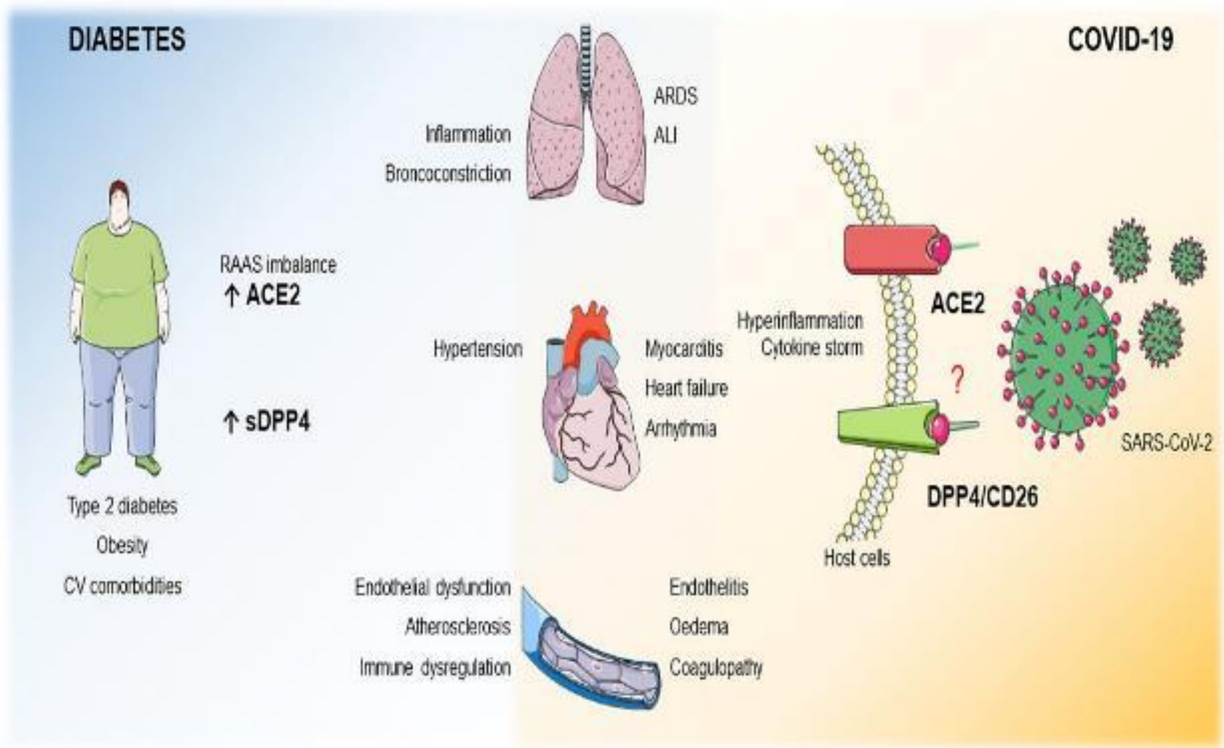
Wang et al. J Med Virol. 2020 Oct 23.

SARS-CoV-2 and DPP4

- Inflammation plays a key role in SARS-CoV-2 infection
- Dipeptidyl peptidase 4 (DPP4/CD26) is expressed ubiquitously in many tissues (incl resp tract ad immune cells)
- DPP4 identified as an *evolutionarily conserved functional receptor* for the spike protein of MERS-CoV
- Polymorphisms in DPP4 reduced MERS-CoV entry Monoclonal Ab to DPP4/CD26 inhibited MERS-CoV entry
- Degrades incretins such as glucagon-like peptide 1 (GLP-1) → ↓incretin effect → net effect = ↑glycemia
- DPP4 Immune function: cytokine secretion, antibody production, immunoglobulin class switching, CD4+ T cell activation
- DPP4 Important in inflammatory response

Raj et al. Nature. 2013
Klein-Weber et al. Emerg Microbs Infect. 2020
Ohnuma et al. J Virol. 2013

SARS-CoV-2 and DPP4



Valencia et al. Front Pharmacol. 2020

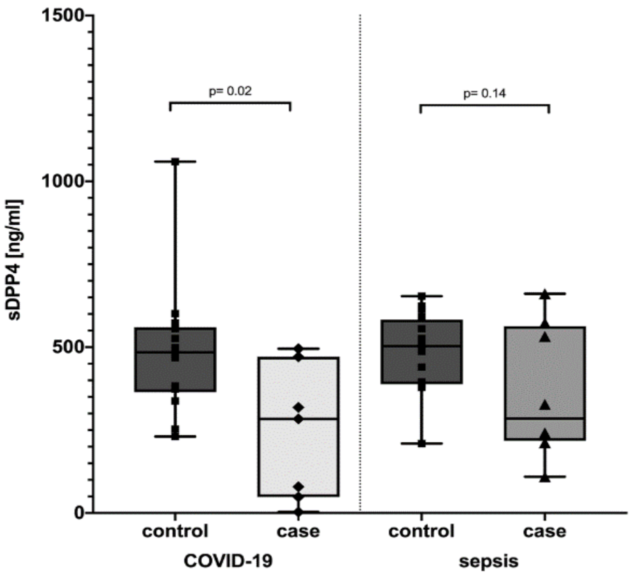
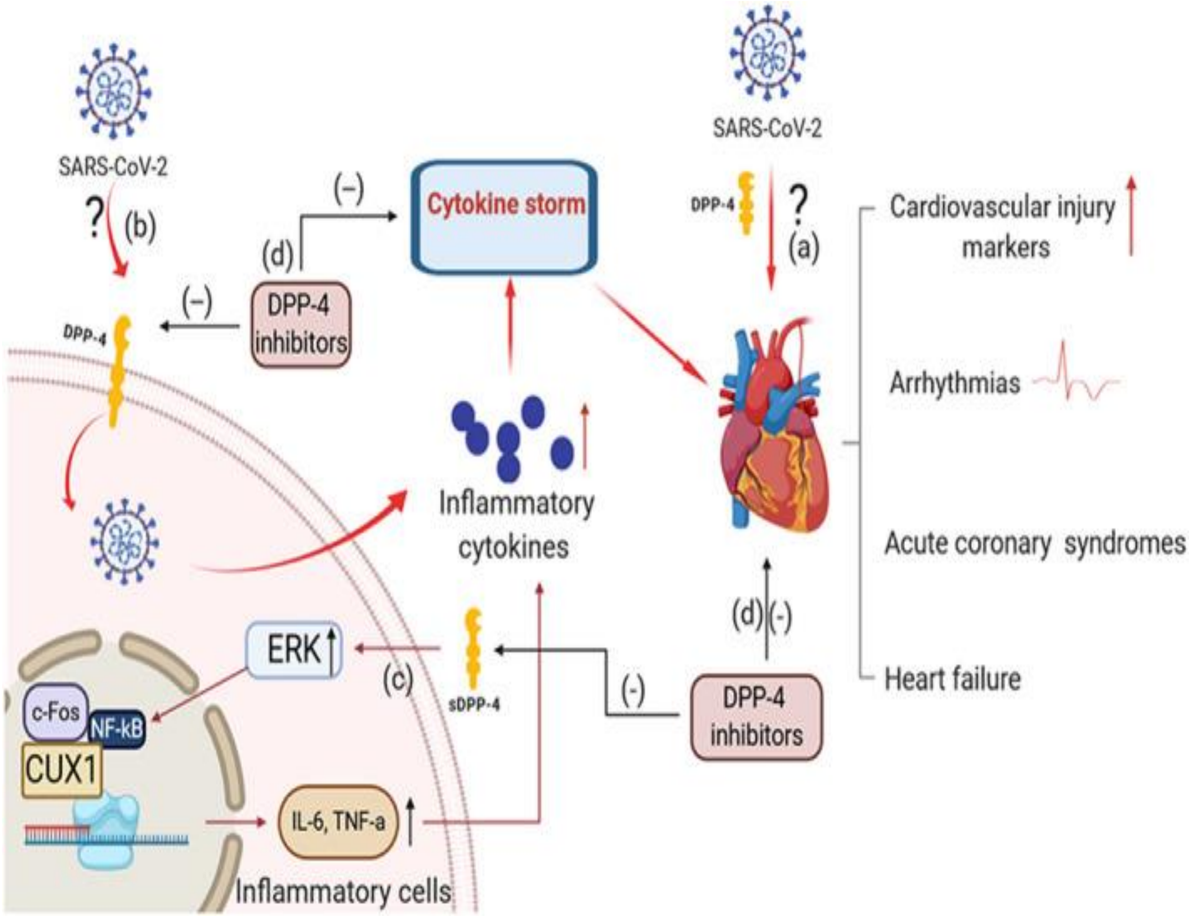


Fig. 1 sDPP-4 in patients suffering from COVID-19 and matched healthy controls, as well as in sepsis patients and matched healthy controls. sDPP-4 is significantly reduced in patients suffering from acute COVID-19 infection compared to healthy controls (p = 0.02). sDPP4 is not significantly reduced in sepsis patients, compared to healthy controls (p=0.14). Statistical significance was tested using t-Tests

Schlicht et al. Int J Obesity.2020

SARS-CoV-2 and DPP4 Inhibition



Du et al. J Cel Mol Med. 2020.
Yang et al. Diabetes Metab Res Rev. 2016.

- DPP4i reduce inflammation by reducing NF-kappa-B signaling pathway
- About 10% of DPP4i users have viral URIs, but meta-analysis demonstrated that it is not associated with increased risk of URIs against active comparators/placebo
- DPP4i improves glucose tolerance
- DPP4i suppresses T cell proliferation and pro-inflammatory cytokines
- ?Modify SARS-CoV-2-DPP4 interaction and inhibit viral entry?
- Clinical trials are in progress

SARS-Cov-2 and glp-1R Agonists

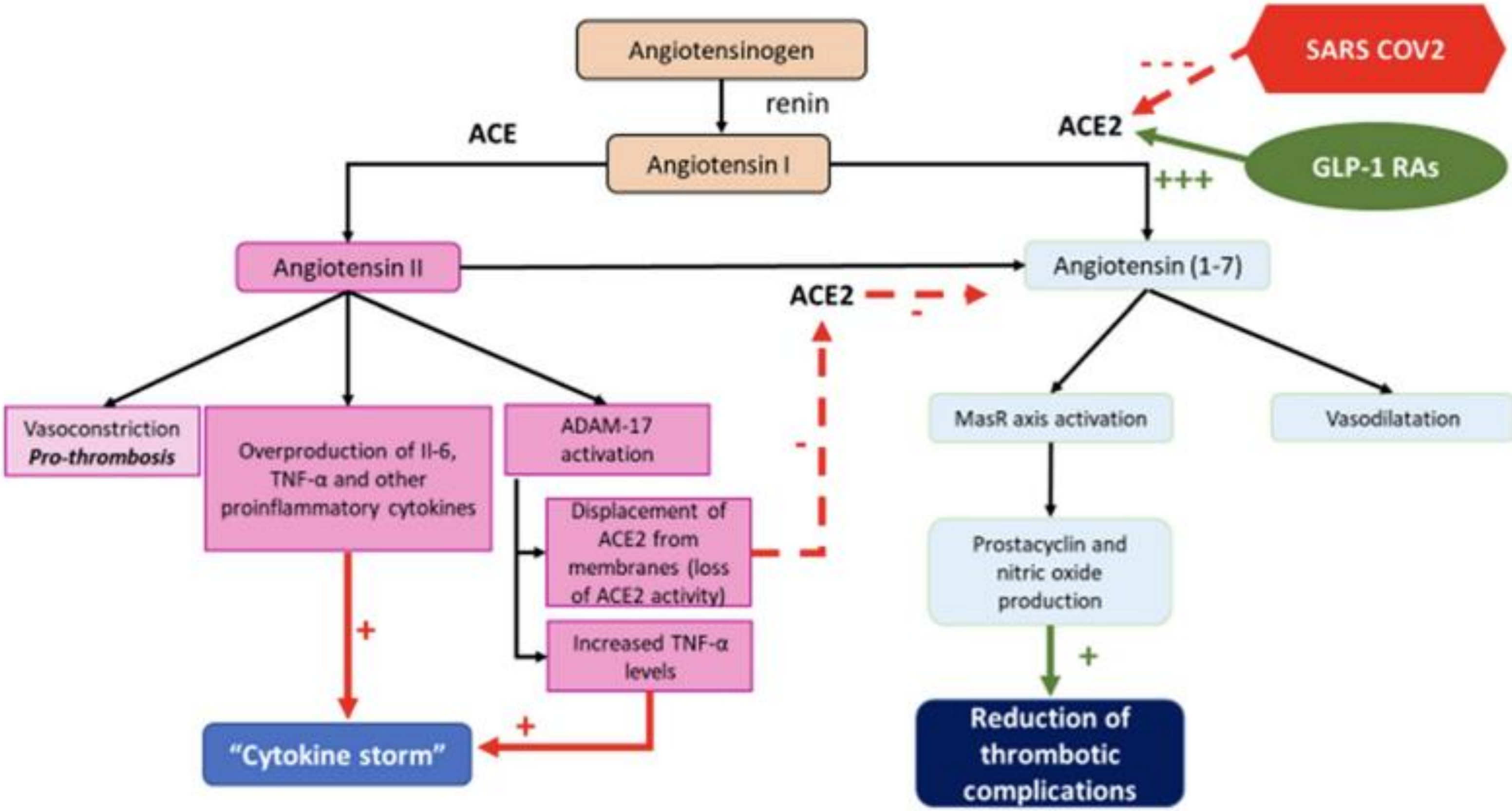


Fig. 1 Possible role of dysregulation of RAS during SARS-CoV-2 infection at lung level and potential beneficial effects of GLP-1 RA_S therapy (see text for details)

Monda et al. Diabetes Ther. 2020.

HAWAI'I PACIFIC HEALTH | HAWAI'I HEALTH PARTNERS

CORONADO Trial

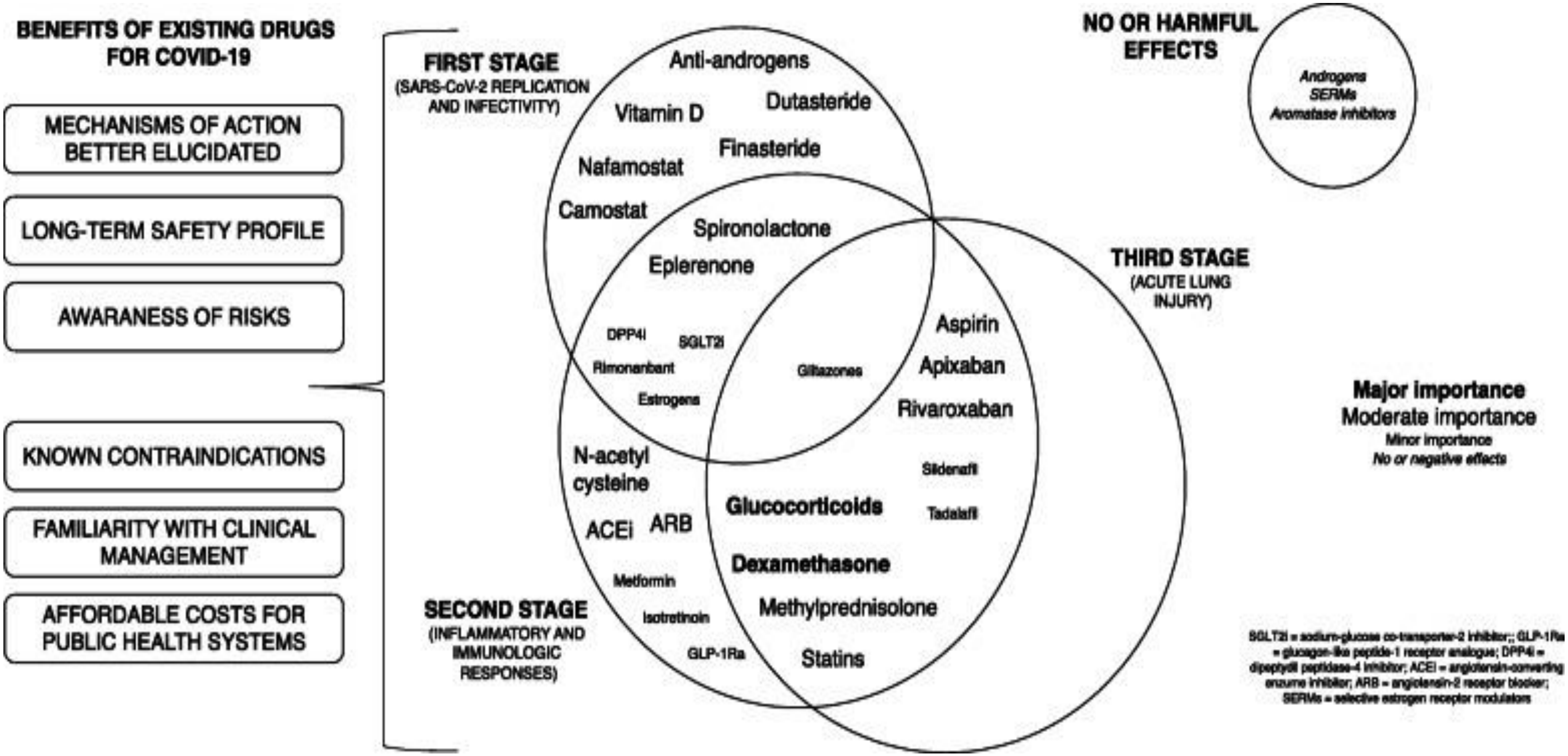
Diabetologia (2020) 63:1500–1515 1505

Table 1 (continued)

Clinical features	Number of people with available data	All	Primary outcome ($n = 382$) OR (95% CI)	Death ($n = 140$) OR (95% CI)
Comorbidities				
Heart failure	1206	140/1206 (11.6)	0.78 (0.52, 1.17)	2.28 (1.42, 3.66)
NAFLD or liver cirrhosis	1107	119/1107 (10.7)	1.23 (0.81, 1.86)	0.70 (0.34, 1.41)
Active cancer	1282	194/1282 (15.1)	1.08 (0.77, 1.50)	1.55 (0.99, 2.42)
COPD	1278	133/1278 (10.4)	0.96 (0.64, 1.43)	1.36 (0.80, 2.32)
Treated OSA	1189	144/1189 (12.1)	1.44 (0.99, 2.08)	1.81 (1.12, 2.93)
Organ graft	1302	38/1302 (2.9)	1.14 (0.57, 2.28)	0.46 (0.11, 1.93)
End stage renal failure	831	60/831 (7.2)	0.66 (0.35, 1.27)	0.62 (0.24, 1.60)
Routine treatment before admission				
Metformin	1317	746/1317 (56.6)	0.95 (0.75, 1.21)	0.59 (0.42, 0.84)
Sulfonylurea/glinides	1317	367/1317 (27.9)	1.03 (0.79, 1.34)	0.74 (0.49, 1.13)
DPP-4 inhibitors	1317	285/1317 (21.6)	1.01 (0.75, 1.34)	0.85 (0.55, 1.32)
GLP1-RA	1317	123/1317 (9.3)	1.36 (0.92, 2.01)	0.64 (0.32, 1.29)
Insulin	1317	504/1317 (38.3)	1.01 (0.79, 1.29)	1.71 (1.20, 2.43)

Cariou et al. Diabetologia. 2020

Potential Repurposing of Existing Endocrine-related Drugs for COVID-19



Cadegiani. BMC Endocr Disor. 2020.

My Diabetic Patients with COVID-19

PATIENT A

- Age 64
- BMI 26
- ~~A1c 7.2%~~ (typically < 7%, increased in pandemic)
- Other comorbidities: Hypertension, Hyperlipidemia
- DM meds: Jardiance, Januvia, Glipizide ER, rosuvastatin, gemfibrozil,
- Overall fitness: Good fitness, highly mobile/active, goes surfing frequently, exercises regularly

PATIENT B

- Age 56
- BMI 45 (initial BMI 52)
- ~~A1c 8.0%~~ (typically 8-12%; less than 9% in past year)
- Other comorbidities: Mild Cardiomyopathy (EF 40%), Hypertension, Hyperlipidemia, NASH, OSA
- Notable meds: Jardiance, Tresiba, Ozempic, lisinopril, furosemide, metoprolol ER, rosuvastatin, omeprazole
- Overall fitness: Poor, sedentary lifestyle, zero exercise

What were the risk factors and modifiers?
Could we have done anything to save Patient A?

Neonatal Care During the COVID-19 Pandemic: Kapi‘olani Medical Center’s Experience

Kara Wong Ramsey, MD
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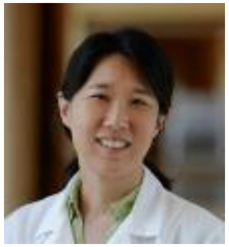
Hawai‘i Pacific Health Medical Group
Assistant Professor, John A. Burns School of Medicine, University of Hawai‘i



Lynn Iwamoto, MD
Neonatologist, Kapi‘olani Medical Center for Women and Children
Hawai‘i Pacific Health Medical Group
Associate Professor, John A. Burns School of Medicine, University of Hawai‘i

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Objectives

- Describe characteristics neonatal infection with COVID-19
- Review the American Academy of Pediatrics Guidelines for Management of Neonates Born to Mothers with COVID-19
- Review recommendations for breastfeeding
- Examine international trends in premature birth rate
- Examine trends in admissions of premature infants at Kapiʻolani's NICU

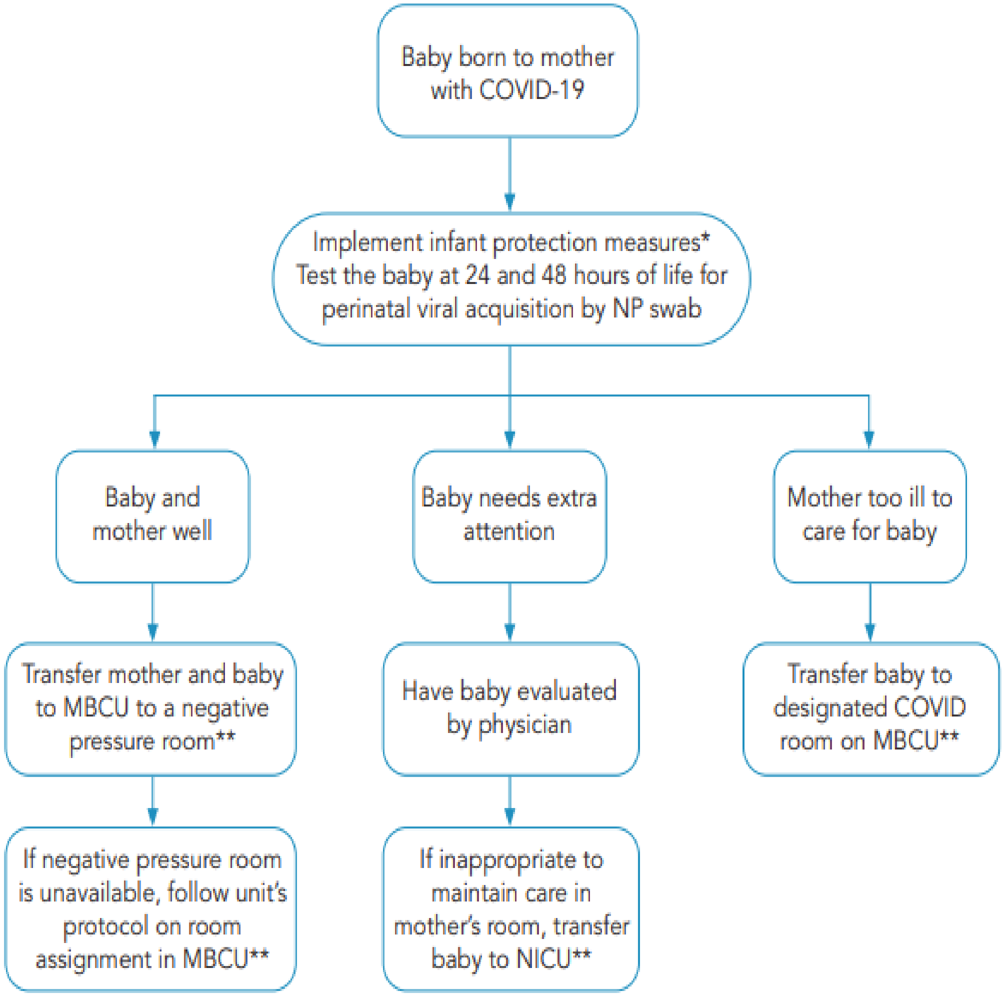
COVID-19 and Neonatal Infection

- Early initial publications from China did not show positive PCR tests in newborns of COVID-19 mothers but had followed strict policies of immediate separation after birth and limitation of breastmilk
- Several reports of neonates with positive PCR tests requiring hospitalization for respiratory distress, fever, poor feeding, diarrhea or vomiting
  - BMJ 2020 Review: 44 neonates mostly term infants in China and Italy
    - 25% asymptomatic, 25% required respiratory support
  - Lancet 2020: 66 infants in UK
    - 24% preterm, 36% required respiratory support
- April 2020 American Academy of Pediatrics (AAP) and CDC: consider separation of neonate and mother after delivery but encouraged provision of expressed breastmilk

Neonatal Management for COVID-19 Positive Mothers

- 2020 AAP Section on Neonatal Perinatal Medicine Nationwide Database (270 hospitals, 47 states, 18% of nation's births)
- 1500 mother infant dyads
  - 2-5% infants positive at 24-96 hours of life
  - No difference in rate of infection between rooming in versus separation
- July 2020 AAP Recommended mothers and infants room in (if no other medical contra-indications)
- September 2020 database: 3300 dyads
  - Highest rate of infection (7.4%) in infants whose mothers were positive within 4-7 days of delivery and required hospitalization for COVID-19 treatment compared to 1.4% overall
- November 2020 database: 4241 dyads
  - 78% of mothers asymptomatic, Most infants born full term
  - 58% infants roomed in, 24% admitted to NICU
  - 14% of infants with ill symptoms (fever, respiratory symptoms, GI symptoms)
    - However did not differentiate from other etiologies of symptoms, including problems related to prematurity

Management of Infants Born to COVID-19 Mothers at Kapi‘olani Medical Center



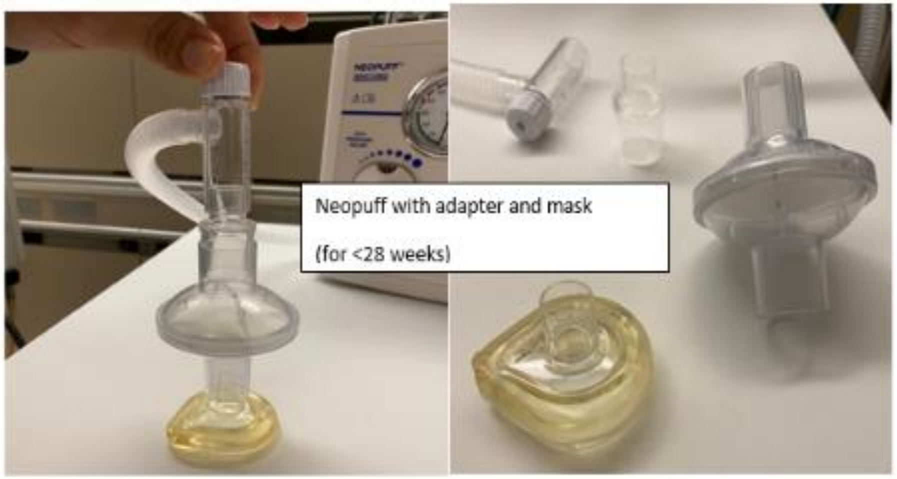
*Staff observes droplet precautions
-Mother wears mask and performs hand hygiene before handling infant
-Breastfeeding and provision of breastmilk encouraged
-When mother not handling infant, infant to remain in bassinet as far away as possible from mother in the room

**NICU admission:
-Transported in isolette
-Airborne precautions if infant requires positive pressure support
-No PUI/COVID-19 positive visitors, including parents

Discharge considerations:
-No advantage to early discharge, may lead to increased problems with medical support and access
-AAP recommends follow federal/state guidelines for routine screening (newborn screen, hearing screen, critical congenital heart disease screening)
-If baby positive for COVID-19 but asymptomatic: Discharged when otherwise medically ready with close follow up over the first 14 days

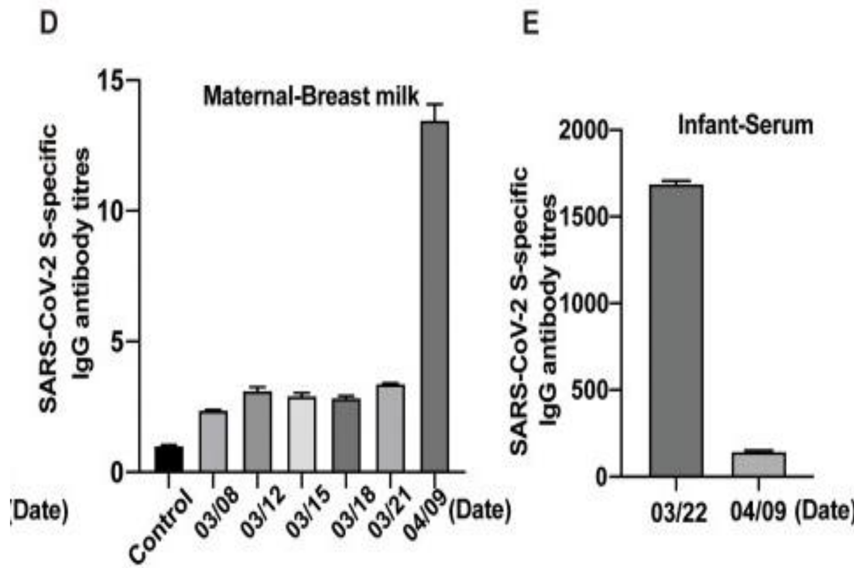
Neonatal Resuscitation for COVID19 Mothers

- Airborne precautions for resuscitation team
  - Double gown
- Viral filter for positive pressure support
- Baby to be transported in isolette



Breastmilk of COVID-19 Positive Mothers

- WHO Systematic Review June 2020: 3 of 46 COVID-19 positive mothers with breastmilk positive RT-PCR
  - 1 of 3 infants became positive on day 11 and admitted for respiratory distress
  - Unclear if infection transmitted through breastmilk or respiratory secretions from mother
- No clear cases of transmission of infection through breastmilk
- Antibodies in breastmilk may protect infant from future infection
- AAP, WHO and CDC recommend continued support of breastfeeding and expression of breastmilk



Dong et al *Emerg Microbes Infect* 2020

Premature births and COVID-19 Pandemic

- Netherlands 2020 (2 months prior and after lockdown)
  - Difference in regression discontinuity analysis: OR 0.77 (0.66-0.91)
  - When stratified by gestational age: Only significant in 32-36 weeks gestational age
  - Reductions primarily occurred in higher socioeconomic status population but effect modification analysis not significant
- Philadelphia (US) 2019 vs 2020
  - Decrease in preemies <37 weeks (OR 0.75 CI 0.57-0.99)
  - Decrease in iatrogenic preterm birth <34 weeks (OR 0.4, CI 0.21-0.75)
- Denmark 2015-2019 vs 2020
  - Decrease only among preemies <28 weeks: OR 0.09 (0.01-0.40)
- Ireland 2001-2019 vs 2020
  - Increased Very Low Birth Weight preemies rate ratio 3.77 (1.21-11.75)
  - No increase in stillbirths or miscarriages
- London (UK) 2019 vs 2020
  - no change in preemies <37 weeks
  - Increase in still birth 2.38 vs 9.31 per 1000 births (difference 6.93, CI 1.83-12.1)
- Nepal 20202 (10 weeks prior vs after lockdown)
  - Increase in still birth from 14 to 21 per 1000 births
  - Increase in preemies <37 weeks 16.7% vs 20% (p<0.01)

Possible reasons for the decrease in the incidence of PTB during COVID-19 pandemic
- Less stress and anxiety: work from home
- Other work changes: no shift work, no long hours, and less physical work
- Better support systems: partner and family
- Better nutrition
- More exercise
- Better hygiene and fewer social interactions: fewer infections
- Less smoking owing to being indoor and fewer chances of drug use because of the lockdown
- Less car driving: less stress and fewer accidents
- Less air pollution
- Government financial assistance
- Fewer medical interventions

COVID-19, coronavirus disease 2019; *PTB*, preterm birth.

Berghella. Preterm birth in COVID-19 pandemic. Am J Obstet Gynecol MFM 2020.

Lancet Glob Health 2020
JAMA 2020
BMJ Glob Health 2020

Points to Remember

- AAP and CDC recommend co-rooming and breastfeeding for infants of COVID-19 mothers based on growing data that the benefits outweigh the infectious risk to the neonate

- Neonatal infection is less common and most are either symptomatic or have mild disease not requiring respiratory support but are more likely to require respiratory support than older pediatric patients

- Numerous proposed hypotheses on why multiple countries have observed changing trends in rates of premature birth before and after the pandemic but the effect is not consistent across various geographical locations

- How are we doing in Hawaii?
  - Let's examine the trends within the state of Hawaii and at Kapiolani Medical Center…

U.S. INTERNATIONAL CANADA ESPAÑOL 中文

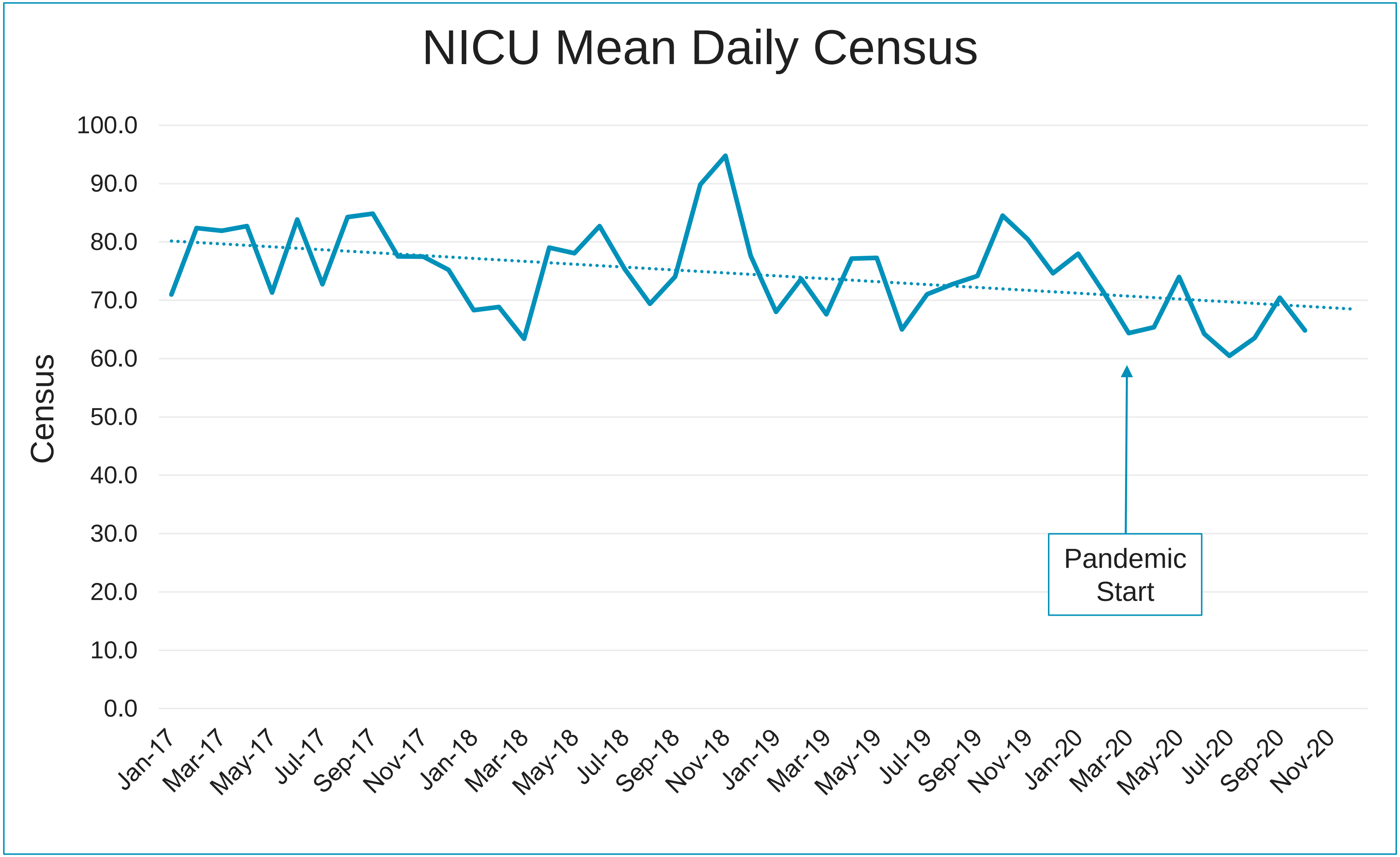
The New York Times

During Coronavirus Lockdowns, Some Doctors Wondered: Where Are the Preemies? 7/19/20

Hospitals in several countries saw dips in premature births, which could be a starting point for future research.

Did Lockdowns Lower Premature Births? A New Study Adds Evidence 10/15/20

Dutch researchers say the "impact was real," adding to hopes that doctors will learn more about factors contributing to preterm birth.


NICU Mean Daily Census
Census
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
Jan-17
Mar-17
May-17
Jul-17
Sep-17
Nov-17
Jan-18
Mar-18
May-18
Jul-18
Sep-18
Nov-18
Jan-19
Mar-19
May-19
Jul-19
Sep-19
Nov-19
Jan-20
Mar-20
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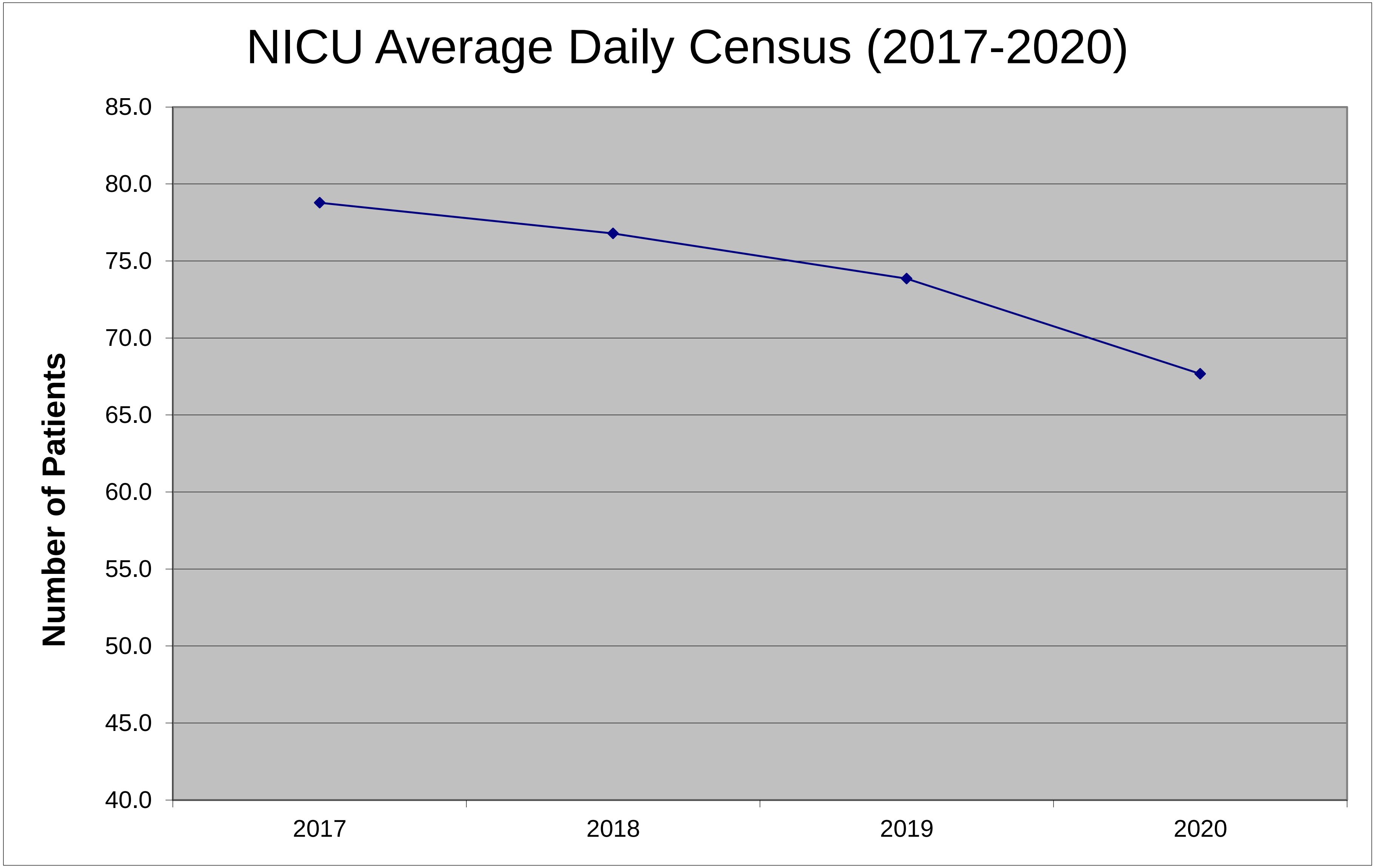
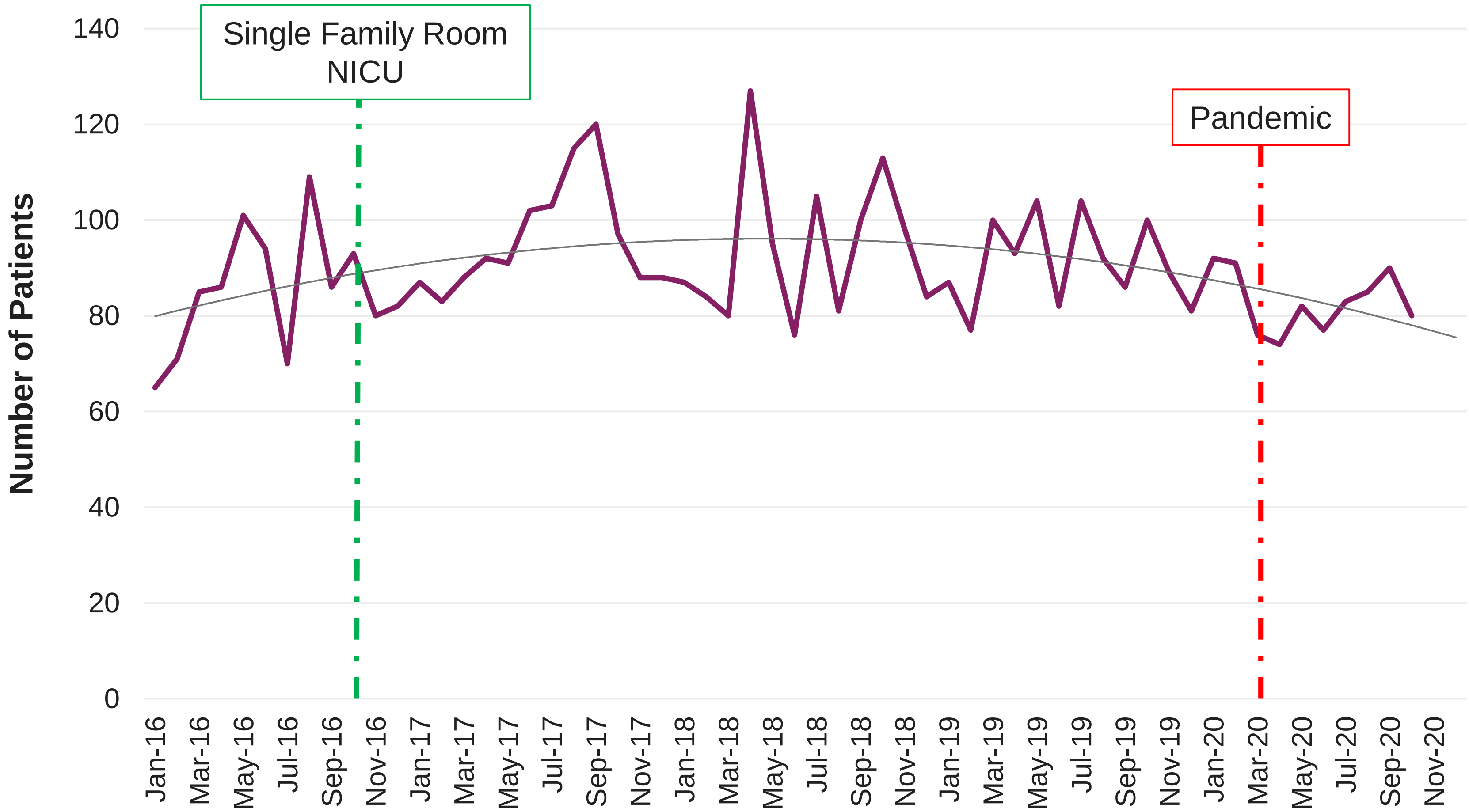
Jul-20
Sep-20
Nov-20
Pandemic Start

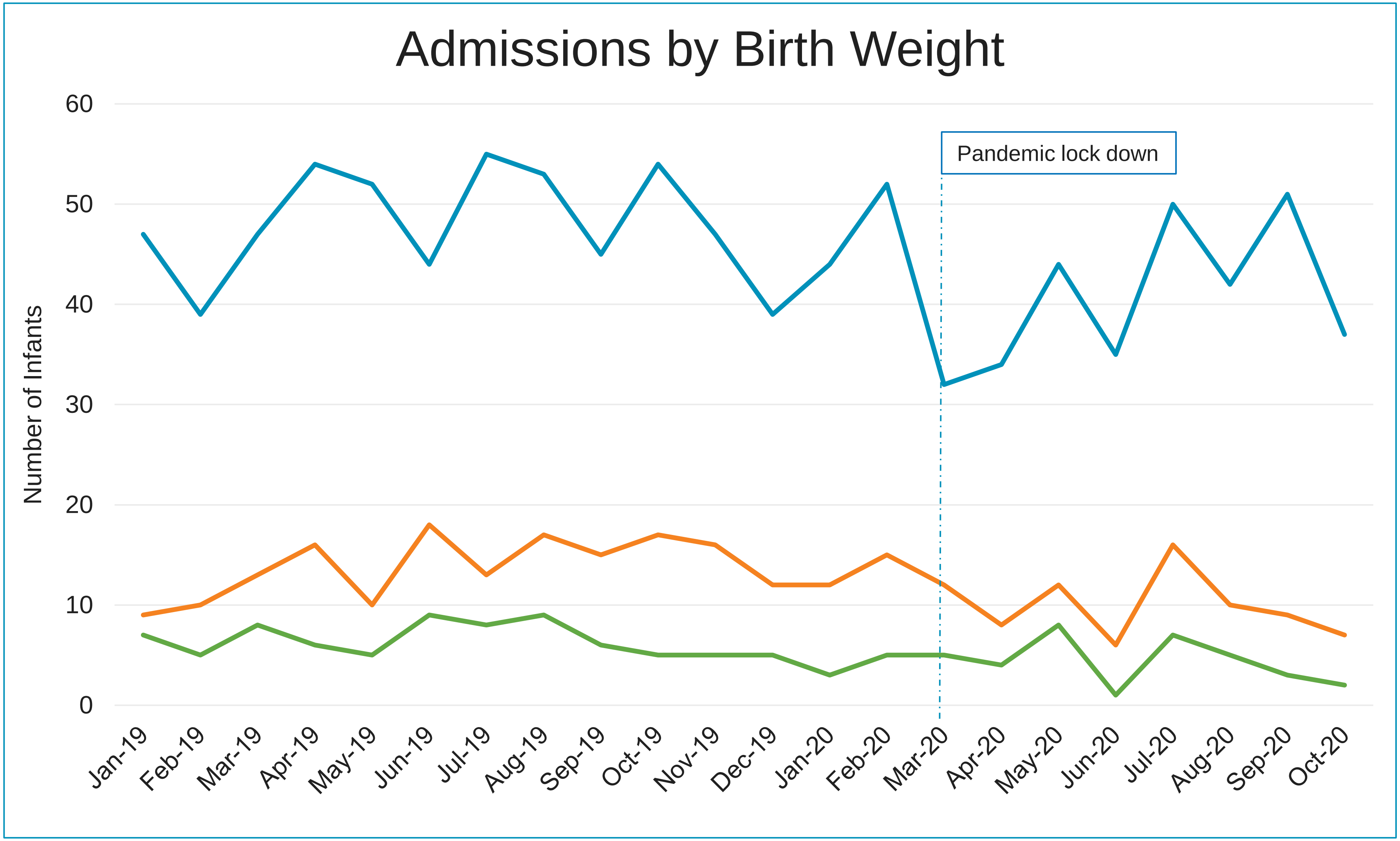

NICU Average Daily Census (2017-2020)
Number of Patients
85.0
80.0
75.0
70.0
65.0
60.0
55.0
50.0
45.0
40.0
2017
2018
2019
2020

Total NICU Admissions



CREATING A HEALTHIER HAWAIʻI

HAWAIʻI PACIFIC HEALTH | HAWAIʻI HEALTH PARTNERS


Admissions by Birth Weight
Number of Infants
60
50
40
30
20
10
0
Pandemic lock down
Jan-19
Feb-19
Mar-19
Apr-19
May-19
Jun-19
Jul-19
Aug-19
Sep-19
Oct-19
Nov-19
Dec-19
Jan-20
Feb-20
Mar-20
Apr-20
May-20
Jun-20
Jul-20
Aug-20
Sep-20
Oct-20

BABY BUST

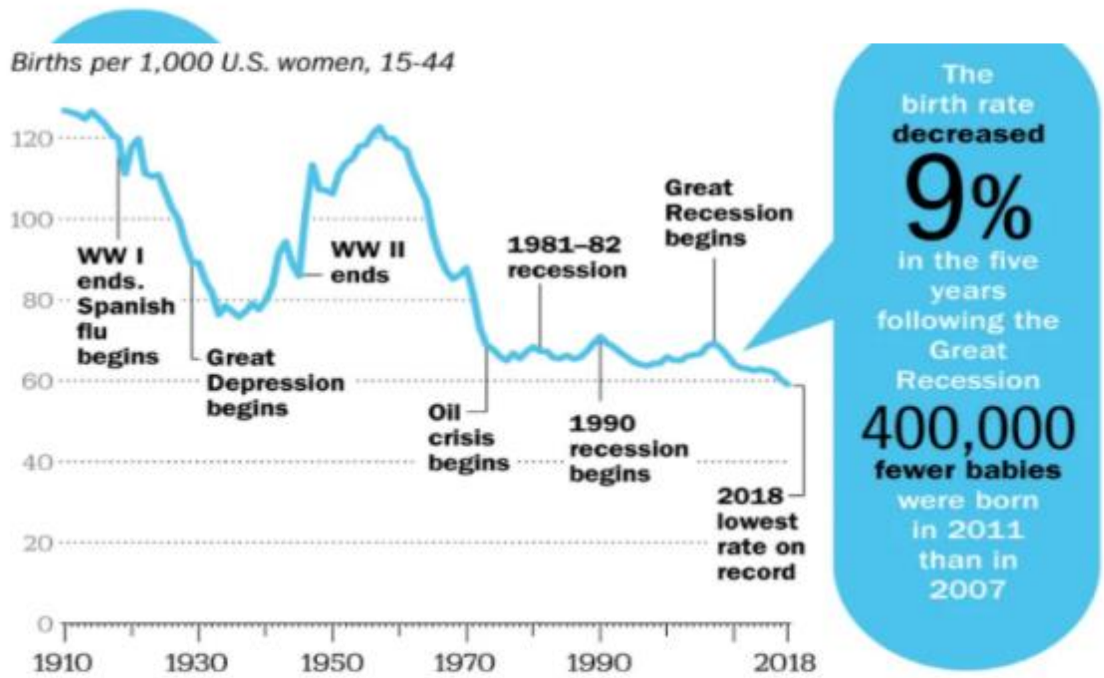
Contrary to some beliefs that lengthy isolation would lead to more babies conceived and born, analysts now predict up to 500,000 fewer births in the U.S. next year

3.8 MILLION
Births in 2019

SOURCE: BROOKINGS, JUNE

3.3 MILLION
Births expected in 2021

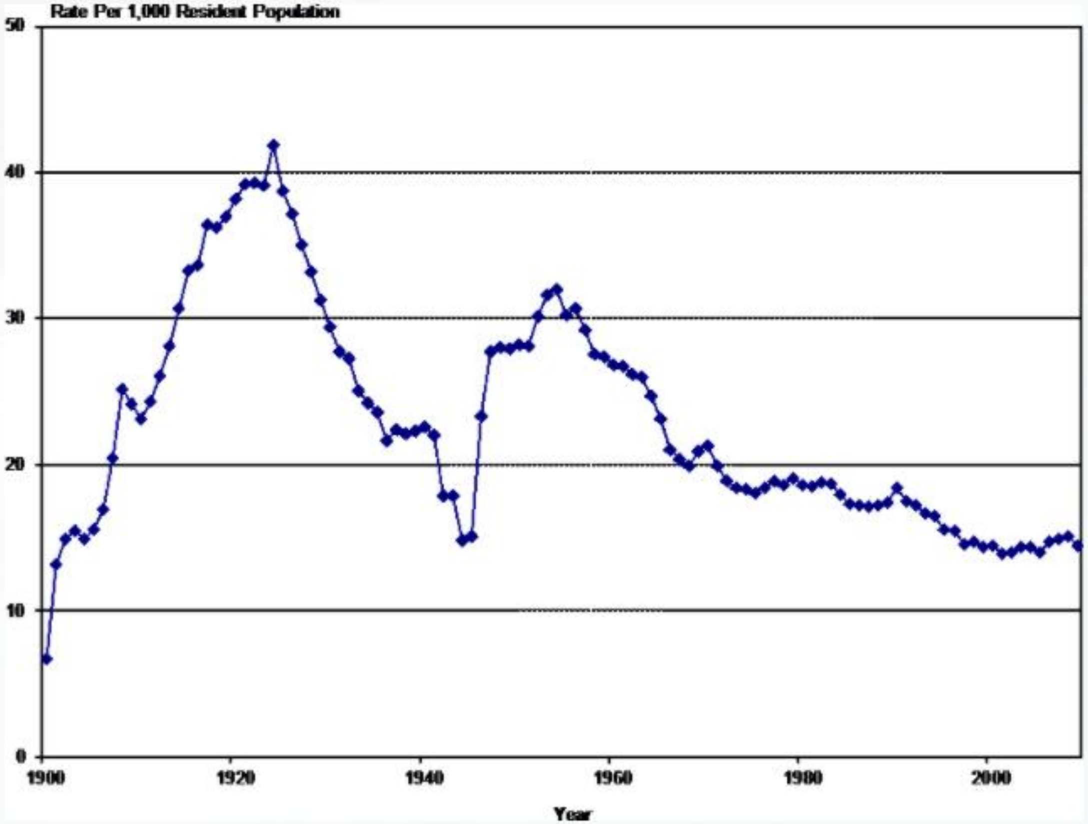
Potential parents may now fear health risks associated with hospital visits, but the birth rate is also linked to confidence in the economy



SOURCES: POPULATION RESEARCH INSTITUTE; NATIONAL CENTER FOR HEALTH STATISTICS

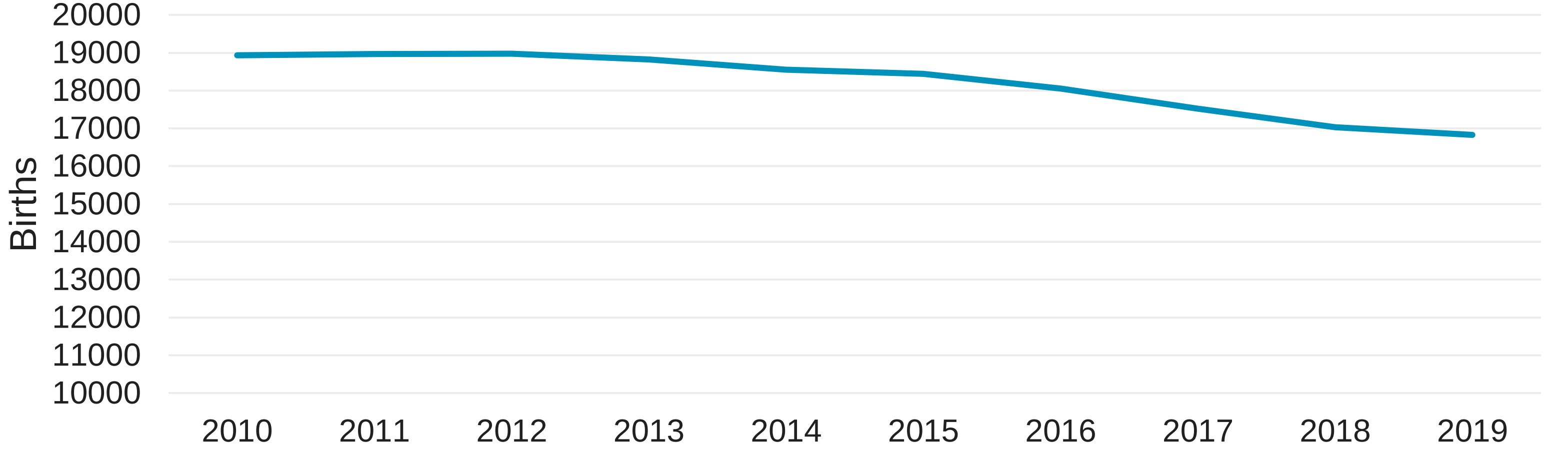
STATE OF HAWAII
DEPARTMENT OF HEALTH
OFFICE OF HEALTH STATUS MONITORING

BIRTH RATE IN HAWAII – 1900 TO 2009

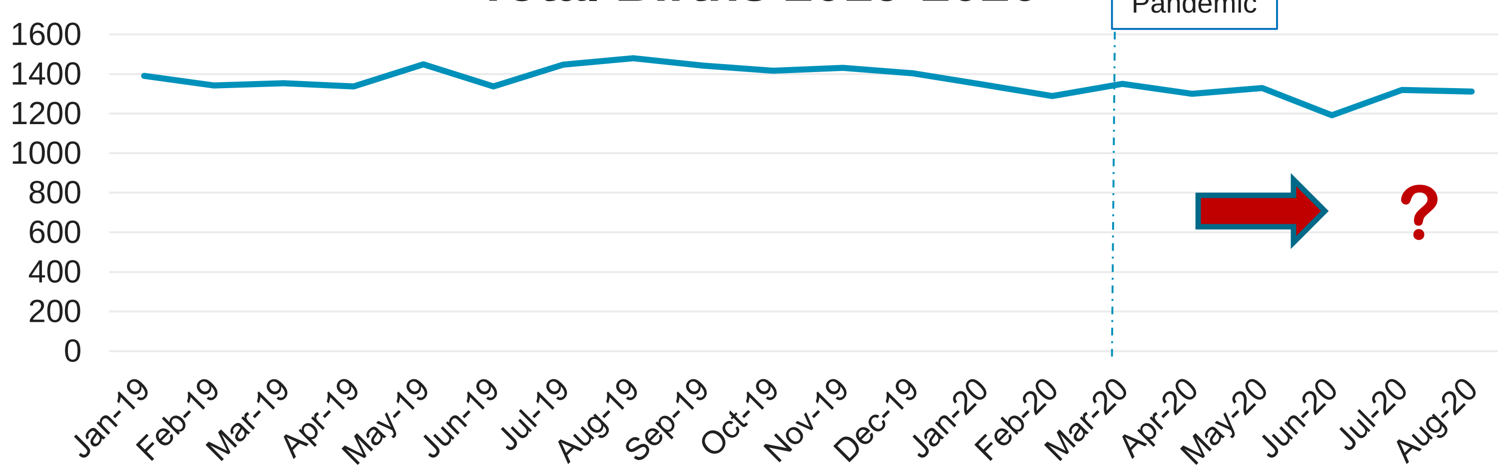


Last Updated on 04/15/2011 By Office of Health Status Monitoring

Total Annual Births: State of Hawaii Pre-pandemic (2010-2019)



Total Births 2019-2020



https://health.hawaii.gov/vitalstatistics/

The Economist | Today | Weekly edition | Menu

April 3, 2020

Graphic detail

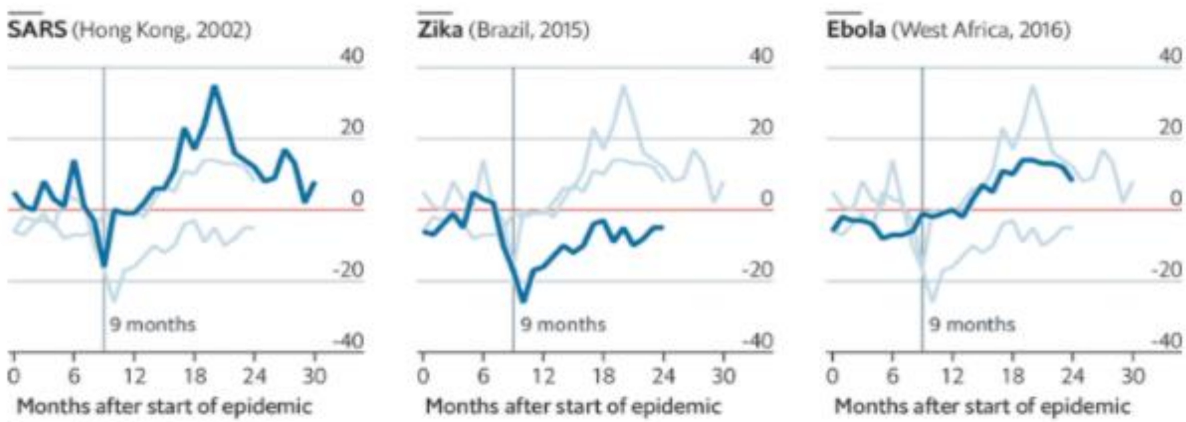
Daily chart

Will the coronavirus lockdown lead to a baby boom?

Deadly epidemics seem to depress birth rates in the short term

Pregnant pause

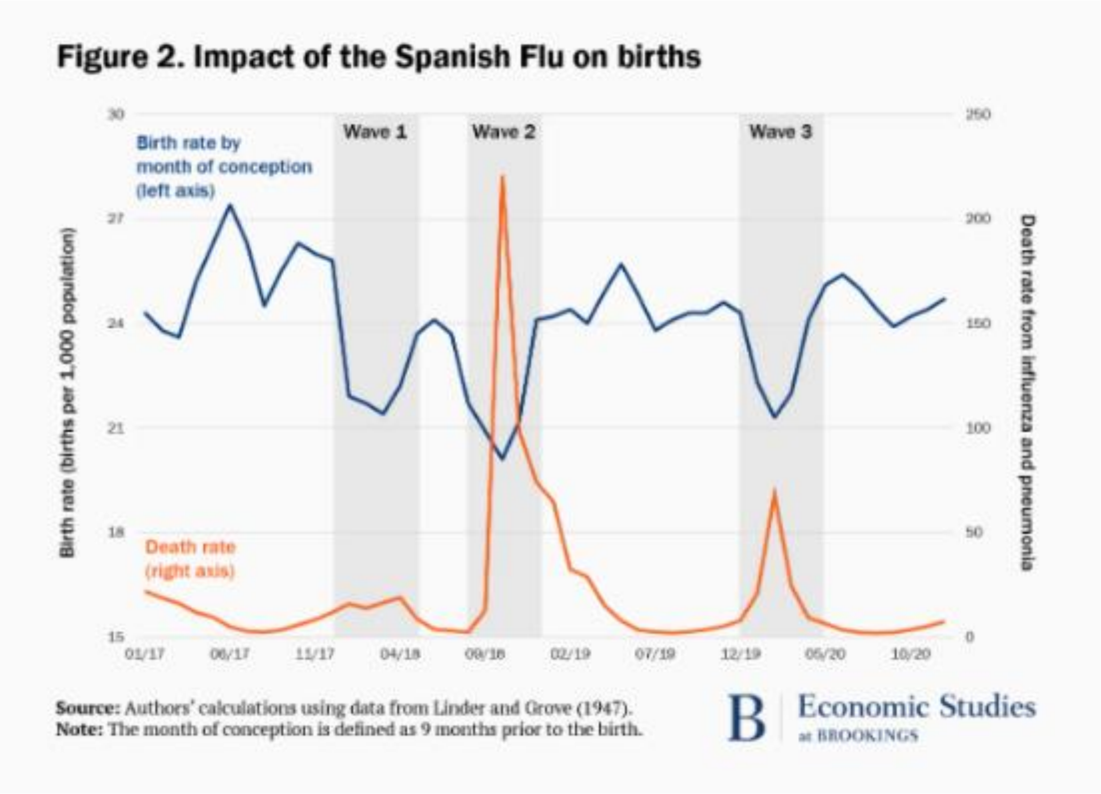
Birth rate, change from seasonal average, %



Source: Institute for Family Studies

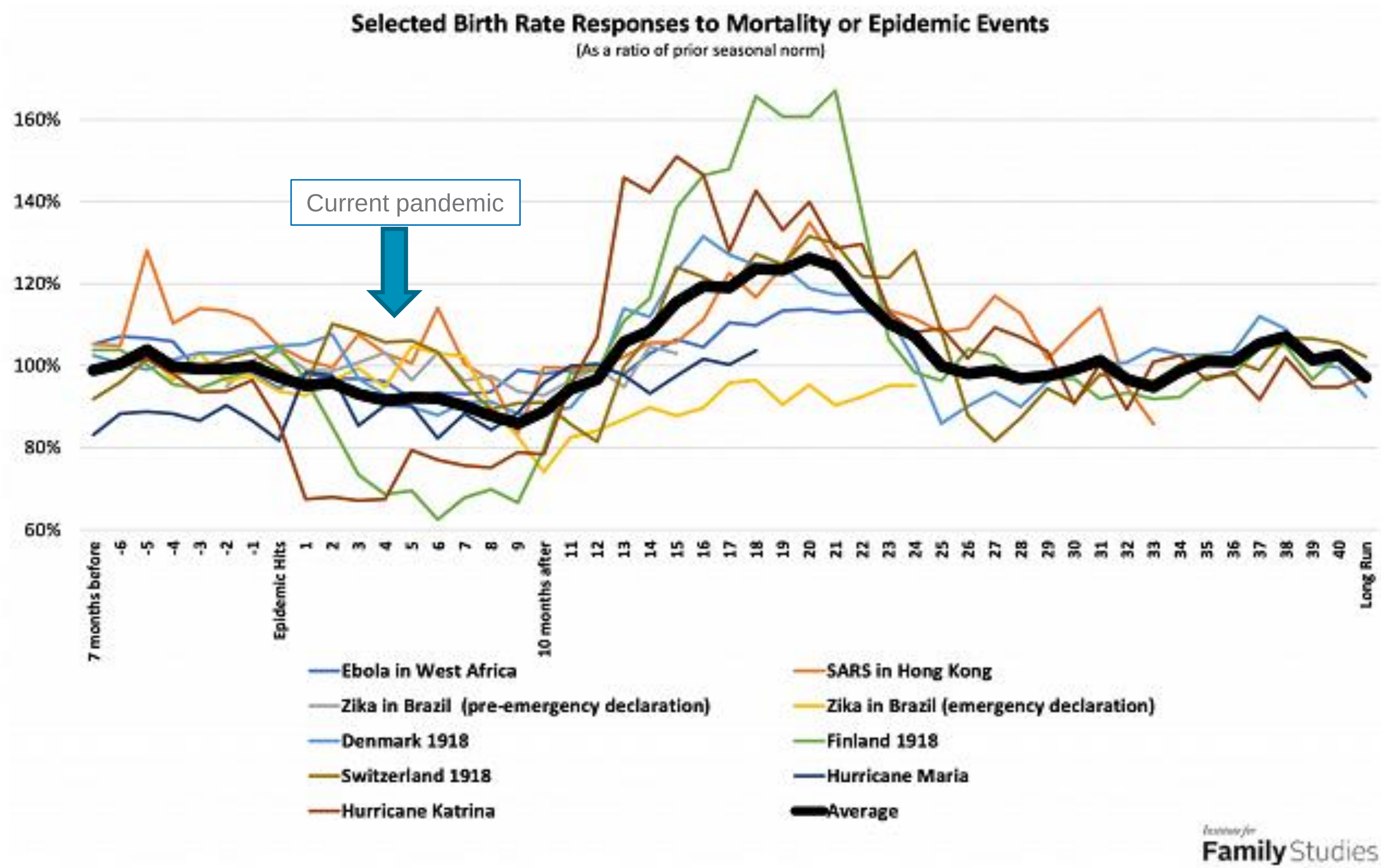
The Economist

https://www.economist.com/graphic-detail/2020/04/03/will-the-coronavirus-lockdown-lead-to-a-baby-boom



- Economic and high mortality impact of Spanish Flu pandemic
  - Anxiety from public health crisis
  - Affected people of childbearing age
- No rebound increase

https://www.brookings.edu/research/half-a-million-fewer-children-the-coming-covid-baby-bust/#:~:text=The%20COVID%2D19%20episode%20will,people%20to%20have%20fewer%20children.



https://ifstudies.org/blog/will-the-coronavirus-spike-births

Summary

- Decrease in NICU admissions and census
  - Decreased preterm/LBW infants
  - No change very low and extremely low birthweight infants
  - Overall decreasing state birth rate

- Impact of pandemic yet to be seen
  - Currently 8-9 months since the start of the pandemic
  - Further decrease in birth rate expected

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- Management of Infants Born to Mothers with Suspected or Confirmed COVID-19. American Academy of Pediatrics. Updated September 9 2020.

Q&A

Next and *last* webinar for 2020*:

Monday, December 7th

5:30 – 6:30 pm

*We will pick up again in the New Year – 2021

Hope you have a Happy Thanksgiving next week!

Thank you!

- A recording of the meeting will be available afterwards.
- Unanswered question?
  - Contact us at Covid19Bulletin@hawaiipacifichealth.org